

Body Contouring

Global Expert Opinion on Cryolipolysis Treatment Recommendations and Considerations: A Modified Delphi Study

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Abstract

Background: Cryolipolysis is an increasingly popular nonsurgical fat-reduction procedure. Published treatment guidance and adverse event (AE) management protocols are limited.

Objective: A modified Delphi study aimed to establish global expert consensus on the use of CoolSculpting (Allergan Aesthetics, an AbbVie Company, Irvine, CA), a noninvasive cryolipolysis treatment system.

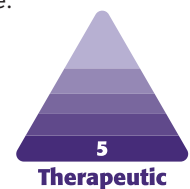
Methods: A literature search informed survey topics for an 11-expert Delphi panel. Panelists completed an online 39-question survey. An interim panel discussion, with open-ended questions and yes/no voting, informed a second survey containing 61 statements, for which panelists rated agreement using a 5-point Likert scale. Topics included treatment outcome and responder definitions, patient evaluation and selection, treatment protocols, patient satisfaction, and AEs.

Results: Panelists achieved consensus on 38 final guidelines and recommendations. They reached moderate to complete consensus on 4 statements on defining responders (ie, patients with a range of visible improvement) and 6 statements on patient factors contributing to treatment outcomes (eg, how well the applicator conforms to patient body region). Panelists defined minimum numbers of treatment cycles to achieve visible clinical outcomes for 12 body regions, with moderate to complete consensus on 31 statements. They achieved a strong to complete consensus on 7 statements about patient satisfaction (eg, importance of patient expectations, visible improvement, and before-and-after photographs). Panelists defined management strategies for AEs, with moderate to complete consensus on 15 statements.

Conclusions: A modified Delphi process yielded multiple guideline recommendations for cryolipolysis, providing a needed resource for the broad range of clinicians who perform this noninvasive fat-reduction procedure.

Level of Evidence: 5

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The number of nonsurgical fat-reduction procedures has been increasing annually.^{1,2} Individuals may favor noninvasive procedures over surgical methods to reduce excess fat, as surgery may involve anesthesiologic risks, infections, pain, reoperations, scars, downtime, and bleeding.³ According to the Aesthetic Society's Aesthetic Plastic Surgery National Databank, nonsurgical fat-reduction procedures totaled 140,314 in 2020 and were among the top 5 nonsurgical procedures performed in 2019.^{1,2}

Cryolipolysis (CoolSculpting; Allergan Aesthetics, an AbbVie Company, Irvine, CA, USA) is a nonsurgical and noninvasive procedure that freezes subcutaneous fat cells through the application of slow, intense, controlled cooling, after which these cells undergo apoptosis and elimination from the body.⁴⁻⁶ It is increasingly sought as an alternative to surgical fat-removal procedures because it may produce high patient-satisfaction levels without the same risks and recovery time.^{3,7-14}

CoolSculpting received initial US Food and Drug Administration approval in 2010 for fat reduction in the flanks and abdomen.^{12,15} CoolSculpting is cleared for fat layer reduction through cold-assisted lipolysis in Europe, Canada, Australia, and Malaysia. In the United States, it is currently indicated for the treatment of fatty areas in the flanks, abdomen, thighs, submental and submandibular regions, bra strap region, back, underneath the buttocks, and upper arms.^{4,15,16} Clinical knowledge and technical understanding of cryolipolysis are still developing. Product labeling and existing literature provide limited technical direction and treatment guidance.^{7,16-19} The literature lacks comprehensive direction on techniques to ensure symmetrical outcomes in particular body areas, achieve optimal placement of the cooling applicators to target fat layers, improve procedural time, screen patients for treatment, identify responders, and develop effective protocols for optimal numbers of treatment cycles and sessions, follow-up periods, durations between treatment sessions, patient satisfaction, and adverse event (AE) prevention and management.²⁰ The authors of this publication sought to provide expert consensus guidance for defining CoolSculpting treatment outcomes and responders, understanding patient selection and evaluation criteria, establishing treatment protocols, addressing patient satisfaction, managing AEs, and decision making on cryolipolysis as a treatment modality.^{7,20-26} A modified Delphi approach was the selected study method. These are the first expert consensus recommendations on cryolipolysis to be published in the literature.

METHODS

Delphi Process and Participants

The study sponsor recruited 11 global experts in cryolipolysis, including clinicians in the fields of dermatology,

plastic surgery, cosmetology, and aesthetics, to participate in a modified Delphi process (Figure 1). The expert panel was composed of 5 dermatologists (45.5%), 4 plastic surgeons (36.4%), 1 cosmetic doctor (9.1%), and 1 aesthetic physician (9.1%). The experts had an average of 18.5 years working in their current setting, with 10.3 years on average of CoolSculpting use and experience treating an average 33.9 patients per month with the device. Furthermore, only 1 of the 11 experts did not have experience with other devices for temperature-based fat reduction, representative of the overall expertise with cryolipolysis. The Delphi method is an established technique for reaching expert consensus that uses an initial inquiry to collect data, rounds of questioning, formulation of items for consideration, and reformulation of items to establish an agreement.²⁷ This study used a modified approach by prespecifying 2 rounds of surveys and predetermining thresholds for reaching an agreement, and by including a non-anonymous, one-time, interim meeting in which experts discussed and ranked topic items to help drive consensus. The sponsor used the services of a third-party scientific consulting agency, Endpoint Outcomes, to manage the Delphi process.

Literature Search

The panel chairperson developed the first round of survey questions in coordination with the third-party consultant and the study sponsor. The consultant conducted a MEDLINE literature search in February 2020 for publications in the last 10 years on fat-freezing and cryolipolysis in human adult populations to identify the topics for questions and options for answer choices for the initial survey. The intent of this survey was to capture expert consensus on best practices for patient selection, treatment experience, and AE management with cryolipolysis. The literature included review articles, summary documents, and publications synthesizing information across other sources, covering treatment procedure standards, patient selection criteria, and/or methods for assessing treatment efficacy and/or AE management; excluded from consideration were animal and pediatric studies, commentaries on other articles, publications about clinical trials and other specific studies, and publications lacking abstracts.

Survey Development, Administration, and Discussion

The 11 panelists completed the first-round survey, which consisted of 39 free-response and multiple-choice questions and was distributed through email and administered electronically using SurveyMonkey (San Mateo, CA). The survey had 7 sections: panelist demographics, defining cryolipolysis outcomes, patient evaluation and selection, treatment protocols for each body region being treated, management of patient satisfaction, AE management, and

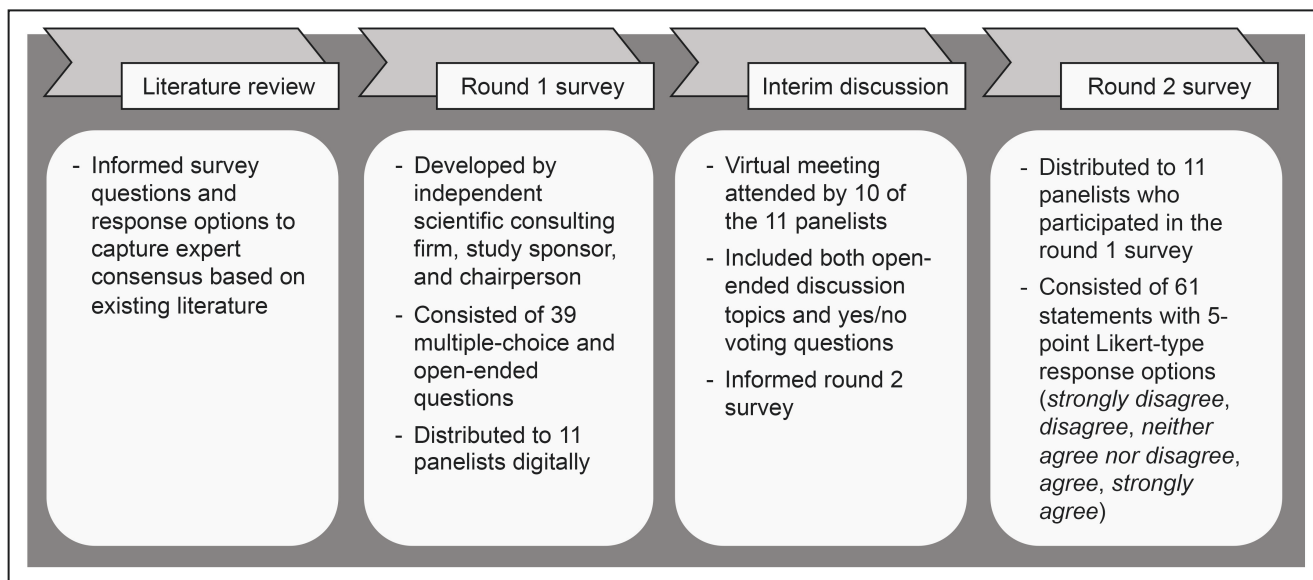


Figure 1. Modified Delphi process.

selecting cryolipolysis as a treatment modality. Response options for the multiple-choice questions were generated from the literature review and panel chairperson feedback. Response options for multiple-choice questions included drop-down numerical responses, scale-based choices (such as not important, somewhat important, and very important), and an “Other [please specify]” option for original responses if existing options did not apply or reflect panelists’ opinions or experience. The survey was closed after completion by all panelists, and panelists’ responses were collated and analyzed. To determine if consensus was met, the frequency with which the responses were reported was calculated from the total number of panelists (N = 11), with a minimum of 7 endorsements (63.6%) as the threshold for consensus. The responses to open-ended questions and any “Other” responses were merged, when possible, using qualitative coding methods and operationalized using ATLAS.ti version 8.0 or higher (ATLAS.ti GmbH, Berlin, Germany). Original responses deemed relevant by the study group were developed into statements to be voted on for endorsement by the panel during the second survey.

The panelists then participated in a virtual interim meeting that included open-ended discussion and yes/no voting on questions pertaining to the results of the first survey. After the panelists were polled on these questions, they viewed the results of their votes on screen and discussed the findings. This discussion informed the development of topics, questions, and response options for a second survey. The goal of the second survey was to achieve consensus on all outstanding topics from the first survey and interim discussion. The second survey, also administered electronically through SurveyMonkey to the 11 panelists, consisted of 61 statements designed to drive consensus and generate treatment guidelines and

Table 1. Predetermined Thresholds to Evaluate Consensus in Cryolipolysis Delphi Panel

Strength of consensus	Threshold for percent and number of panelists (of 11 Total)
Complete	100% (11)
Strong	81.8% to 90.9% (9-10)
Moderate	63.6% to 72.7% (7-8)
Consensus not achieved	0% to 54.5% (0-6)

recommendations related to cryolipolysis. Panelists rated their level of agreement with 60 of these statements using a 5-point Likert-type scale (strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree).

Consensus Methodology

When completing both surveys and considering questions during the interim discussion, panelists were asked to consider their overall experience with cryolipolysis—ie, to approach questions from the perspective of treatment experience with about 80% of their patients. To achieve consensus, endorsements were required from a minimum of 7 panelists; Table 1 summarizes the full criteria for establishing consensus.

RESULTS

Literature Review

The literature search generated 104 articles, and the study sponsor provided an additional 23 references. All articles were reviewed for relevance, and 23 were ultimately

included and informed the development of the initial survey. A key finding of the literature review was that the terms “responders” and “nonresponders” were used frequently without guidelines on the criteria for categorizing patients as such. Furthermore, the literature review revealed a lack of published recommendations on measurement techniques for defining outcomes, real-world ranges of cycles per body region, guidance for addressing problems that arise during the procedure, and pre- and post-patient routines and follow-up. No articles recommended a preferred time between treatment sessions or for a treatment follow-up interval.

First-Round Survey

A consultant drafted the first-round survey questions and response options with input from the sponsor, and the Delphi panel chairperson modified and approved the questions and response options. The questions addressed limitations and clinical concerns identified in the literature, such as which body areas can be treated together in the same session; pretreatment and posttreatment routines; activities that should be avoided before treatment; criteria for screening patients to receive treatment; and factors that impact patient satisfaction, including comfort during treatment, cost, downtime, treatment duration, pain tolerance, patient expectations, visibility of improvement, and immediacy of treatment.

The literature review revealed that treatment sessions consisted of overlapping treatment cycles and could involve treatment of multiple body areas. Thus, survey questions and meeting discussions used the terms “treatment” and “treatment session” respectively, defined by the chairperson as the “attachment and run of a single applicator on body area for a prescribed duration” and “a single visit during which one or more treatment cycles are delivered.” It is important to note that during a review of the final list of guidelines and recommendations after the second-round survey, it was determined and emphasized that the term “treatment cycles” should be used instead of treatments, and the language in this report aligns with the preferred terminology.

Survey questions and meeting discussions also referred to AEs identified in the literature as those that impacted treatment, required intervention, or limited patient satisfaction with cryolipolysis, including paradoxical adipose hyperplasia (PAH), lip paresthesia, severe pain, late-onset pain, frostbite, necrosis, increased sensitivity, and nodular infiltration.^{12,28-30}

During the first-round survey, panelists achieved consensus regarding the management of patient satisfaction, without further discussion needed. Panelists reached a strong to complete consensus on 7 statements, including that patient comfort during the procedure has a moderate

impact on satisfaction, whereas improvement that is visible to the patient and aligns with patient expectations has a significant impact. The panelists agreed that additional treatment cycles are an option for patients not satisfied with the initial cryolipolysis treatment. They also strongly recommended that clinicians capture standardized, clinical before-and-after photographs, which can aid in their patients’ recognition of “visible clinical improvement” and thereby enhance patient satisfaction with treatment. Panelists also emphasized that well-defined fat pockets are more commonly associated with more successful clinical treatment outcomes, as the treatment area is more visible; that cryolipolysis has limitations in improving other aesthetic conditions; and that continuous fat pads require additional procedure-related considerations to achieve a successful treatment outcome.

Interim Discussion and Second-Round Survey Outcomes

The interim discussion took place on November 7, 2020, and was attended by 10 of the panelists (1 panelist was absent due to a scheduling conflict). In total, 38 summary statements were generated as a final list of guidelines and recommendations (Table 2). Guidelines and recommendations were derived from the modified Delphi process utilizing the panel’s expert opinions based on their collective clinical experience. Concerning defining treatment outcomes, the panelists categorized different tiers of responders and how best to assess patients in each of these categories, achieving moderate to complete consensus on 4 statements. Panelists agreed on the definition of treatment “responders” as patients who can experience a range of visible improvement, and within this category, “poor responders” as patients who require reassessment or modification of the original treatment plan to demonstrate visible improvement. In contrast, “nonresponders” were defined as a small number of patients who experience no biological response to cryolipolysis treatment (Table 2).

Concerning patient evaluation and selection, the panelists established how specific patient factors contribute to treatment outcomes (the most important driver being how well the applicator conforms to the body region being treated), achieving moderate to complete consensus on 6 statements (Table 2). On treatment protocols, the panelists defined the most feasible/ideal number of treatment cycles for each of the 12 body regions to achieve a clinical visible outcome (Table 3). The panel arrived at the recommended numbers of treatment cycles by indicating their level of agreement with statements in the first survey on treatment cycles and body regions, discussing these results, voting on more specific statements about average numbers of cycles per body region, and summarizing

Table 2. Summary of Final Guidelines and Recommendations

Guidelines and recommendation statements	Subtopic statements	Strength of consensus
Defining outcomes		
1. The term “nonresponder” should be used only to describe a small number of patients who experience no biological response to cryolipolysis treatment.		Complete
2. Within the category of “responder,” patients can experience a range of visible improvement, and a “poor responder” will require reassessment or modification of the original treatment plan to demonstrate visible improvement. This may include additional treatment cycles or alternative treatments.	Patients can experience a range of visible improvement	Complete
	A “poor responder” will require reassessment or modification of the original treatment plan to demonstrate visible improvement. This may include additional treatment cycles or alternative treatments.	Strong
3. Most patients who experience little to no visible response after initial treatment with cryolipolysis would not be considered “nonresponders,” as they would likely respond (either with a visible response or measured by ultrasound scan/caliper measurements) to additional treatment.		Moderate
Patient evaluation and selection		
4. Once a patient has been deemed a candidate for cryolipolysis treatment, a patient’s BMI is generally not a driving factor in determining treatment outcomes but is simply just important to patient selection (ie, patients who fall outside of the current BMI guidelines for cryolipolysis treatment should not be considered candidates for treatment).		Complete ^b
5. Although fat thickness and fat firmness play a role in impacting treatment outcomes, the more important driver of treatment outcomes is whether the applicator can be applied to the area (eg, will the fat fit in the applicator).		Complete ^b
6. Cryolipolysis has limitations concerning targeting all aspects of aesthetic appearance—consideration of scars, cellulite, and stretch marks in the treatment area is important as they can impact treatment outcomes.		Complete
7. Well-defined fat pockets are more commonly associated with more successful clinical treatment outcomes.		Complete
8. Continuous fat pads require additional procedure-related considerations (eg, overlapping applicators, multiple treatments, and selection of most appropriately sized applicator).		Complete
9. Men typically present with more fibrous tissue and can have less visible results due to challenges in administering the treatment (eg, applicator fit).		Moderate
10. Gender affects treatment area selection.		Moderate
Treatment protocols by body region		
11. For body regions that require multiple treatments of the same area, the number of sessions to complete the treatment plan is based on feasibility factors such as: <ul style="list-style-type: none"> • Number of cryolipolysis devices at a clinic, • Patient’s availability, and/or • Patient preference. 		Complete
12. Each patient requires a full body assessment before and throughout a treatment plan, and therefore any body regions may be appropriate for treatment and/or assessment together.		Complete
13. Numbers of treatments typically needed to achieve a clinical visible outcome for specific body regions are summarized in Table 3 .		

Table 2. Continued

Guidelines and recommendation statements	Subtopic statements	Strength of consensus ^a
14. Multiple treatments would likely result in a more visible and clinically successful outcome than one treatment alone.		Complete
15. When multiple sessions are needed, time between treatments may typically range between 4 and 8 weeks.		Strong
16. After completion of a patient's planned final treatment, clinicians should typically wait approximately 8 weeks before assessing the overall outcome of the treatment plan.		Strong
17. When using a vacuum applicator, if a pop-off event occurs with 5 minutes or less remaining in a treatment, the treatment can be considered a complete therapeutic treatment.		Strong
18. When using a surface applicator (eg, CoolSmooth Pro [ZELTIQ Aesthetics, Allergan Aesthetics, an AbbVie Company, Irvine, CA]), if a pop-off event occurs with 10 minutes or less remaining in a treatment, the treatment can be considered a complete therapeutic treatment.		Strong
19. If a thermal event is detected, the need for additional cryolipolysis treatment, if deemed appropriate, should be assessed the next day or after (at least 24 hours after the thermal event).		Strong
20. Postprocedural massage is typically recommended after finishing a cryolipolysis treatment and/or session. Discussing side effects a patient may be experiencing and appropriate patient education and self-care recommendations are also suggested.	Postprocedural massage	Strong
	Discussion of current side effects	Moderate
	Patient education and self-care recommendations	Moderate
21. Time between treatment sessions may vary depending on the body area being treated and the type of fat in that area. Typically, a longer time between treatment sessions may be needed when delivering treatments to the thighs or to areas with more fibrous fat.		Moderate
22. Best practices for preventing procedural problems (eg, pop-off, thermal event) are to: <ul style="list-style-type: none"> • Ensure appropriate applicator selection and placement. • Ensure the patient is comfortable and appropriately positioned during treatment. • Ensure proper strap placement during treatment. • Ensure patient compliance with treatment instructions. • Ensure proper cleaning of site before treatment. • Ensure proper gel pad placement at the time of treatment. • Ensure all staff administering treatment have received the proper training. 	Ensure all staff administering treatment have received the proper training.	Complete
	Ensure appropriate applicator selection and placement.	Complete
	Ensure the patient is comfortable and appropriately positioned during treatment.	Complete
	Ensure proper strap placement during treatment.	Strong
	Ensure patient compliance with treatment instructions.	Strong
	Ensure proper cleaning of site before treatment.	Strong
	Ensure proper gel pad placement at the time of treatment.	Strong
Management of patient satisfaction		
23. Additional treatment cycles are a follow-up option available to patients if they are not satisfied with the result of cryolipolysis treatment due to suboptimal treatment outcomes.		Complete
24. Visibility of improvement and patient expectations are factors that significantly impact patient satisfaction with treatment outcomes.	Visibility of improvement	Complete
	Patient expectations	Strong
25. Patient comfort during treatment moderately impacts patient satisfaction with treatment outcomes.		Strong
AE management (statements 27-36; summarized in Table 4)		

Table 2. Continued

Guidelines and recommendation statements	Subtopic statements	Strength of consensus ^a
Selection of cryolipolysis modality		
37. Advantages of using cryolipolysis as a modality of choice for fat reduction include that the treatment is noninvasive, there is minimal downtime following the procedure, there is evidence supported by clinical trials, there is minimal discomfort during the treatment cycle, the treatment has a strong safety profile, there is an acceptable treatment duration, high patient satisfaction, high versatility (ie, ability to treat multiple body regions), reproducible results, and clinically successful treatment outcomes.	Noninvasive	Complete
	Minimal downtime	Complete
	Evidence supported by clinical trials	Strong
	Minimal discomfort during treatment cycle	Strong
	Safety profile	Strong
	Acceptable treatment duration	Strong
	High patient satisfaction	Strong
	High versatility (ie, ability to treat multiple body regions)	Strong
	Reproducible results	Strong
	Clinically successful treatment outcomes	Moderate
38. The most notable parameters that differentiate the CoolSculpting device from other cryolipolysis devices include: a. Its established safety, b. It is well supported by research and clinical trial evidence, c. It has results that are reproducible, d. Greater overall treatment efficacy, and e. It can be used with a wide variety of applicators.		Complete

^aA moderate consensus rating indicates that 7-8 panelists (63.6% to 72.7%) endorsed a given response, whereas a strong rating indicates that 9-10 panelists (81.8% to 90.9%) endorsed a given response. A complete consensus rating indicates that all 11 panelists endorsed a given response. Consensus was considered not met for recommendations in which 6 or fewer panelists provided endorsement. ^bBased on the interim discussion (no additional exploration during the round 2 survey deemed necessary). AE, adverse event; BMI, body mass index.

recommendations according to the calculated average number of total treatments in an overall treatment plan plus and minus 1 (eg, if the average number of treatments indicated in round 1 was 3, the range included in round 2 would be 2-4). The panelists agreed that, in general, body regions that are larger in size, such as the back and upper abdomen, typically require a greater number of treatment cycles (range, 3-5); most other body regions typically require fewer treatment cycles (range, 2-4). However, ranges of treatment cycles also depend on the bilaterality of body regions—ie, the clinician should ask: Do both the left and right sides of a specific body region on the patient require the same number of treatments to achieve a symmetrical outcome? Panelists also agreed that each patient requires a full body assessment before and throughout a treatment plan, and any region of the body may be appropriate for treatment and/or assessment together depending on the outcome of the assessment. The panel established that “total body assessment” is a method for identifying an appropriate body region or combination of regions for treatment. Multiple treatment sessions will likely result in a more successful treatment outcome, and when multiple sessions are needed, time between treatment may range

between 4 and 8 weeks. In total, moderate to complete consensus on 31 statements related to treatment cycles per body region was achieved (Table 2).

The panelists cautioned that the recommended treatment cycles per body region are not based on “treatment to transformation” or achieving “liposuction-like results,” but rather on the minimums required for an initial visible clinical outcome, and also noted that more cycles may be required to achieve optimal results. Certain regions, such as the abdomen, are highly variable between patients depending on body size, and clinicians may have different approaches to them—ie, they may or may not segment the region into individual treatment areas and may need to administer different numbers of treatment cycles and/or apply different-sized applicators to each side of a region to achieve symmetry (Table 2).

The panelists produced recommendations for times between treatment sessions and between the final treatment and overall outcome assessments as well as best practices for postprocedural routines and procedural problems (Table 2).

Related to AE management and prevention, not all of the panelists were able to share their experience with every

Table 3. Number of Typical Treatment Cycles Recommended to Achieve Clinical Visible Outcome

Body region	Recommended number of treatment cycles	Strength of consensus ^a
Outer thighs (inclusive of left and right)	2-4	Complete
Mid-abdomen	2-4	Complete
Submental/submandibular	2-4	Complete
Mons pubis	1-3	Strong
Banana rolls (fatty areas under buttocks; inclusive of left and right)	2-4	Strong
Upper bra fat (inclusive of left and right)	2-4	Strong
Lower bra fat (inclusive of left and right)	2-4	Strong
Upper abdomen	3-5	Strong
Lower abdomen	3-5	Strong
Back (inclusive of left and right)	3-5	Strong
Inner thighs (inclusive of left and right)	2-4	Moderate
Distal thighs/knees (inclusive of left and right)	2-4	Moderate
Male chest (inclusive of left and right)	3-5	Moderate
Upper arms (inclusive of left and right)	3-5	Moderate
Flanks	4-6	No consensus

^aA moderate consensus rating indicates that 7-8 panelists (63.6% to 72.7%) endorsed a given response, whereas a strong rating indicates that 9-10 panelists (81.8% to 90.9%) endorsed a given response. A complete consensus rating indicates that all 11 panelists endorsed a given response. Consensus was considered not met for recommendations in which 6 or fewer panelists provided endorsement.

AE identified in this research (Figure 2). However, management strategies were collected for all named AEs (Table 4 summarizes their recommendations), and moderate to complete consensus was achieved on 15 statements.

Related to choosing cryolipolysis over other modalities to reduce or remove excess fat, the panelists agreed with strong to complete consensus that the advantages of using cryolipolysis as a modality of choice for fat reduction include that the treatment is noninvasive, there is minimal downtime following the procedure, there is evidence supported by clinical trials, there is minimal discomfort during the treatment cycle, the treatment has a strong safety profile, and there is an acceptable treatment duration, high patient satisfaction, high versatility (ie, ability to treat multiple body regions), reproducible results, and clinically successful treatment outcomes (Table 2).

DISCUSSION

Through a modified Delphi process, the experts generated a comprehensive list of guidelines and recommendations for clinicians who use cryolipolysis devices. The experts' final recommendations align with the results and overall conclusions of the published literature. For example, compared with other modalities for localized excess fat, such as high-intensity focused ultrasound and shock waves, reviews of the scientific literature show more statistically significant data in support of the effectiveness of cryolipolysis as a treatment modality.²⁴ Furthermore, clinical practice

experience suggests that cryolipolysis is safe and produces high patient satisfaction without the risks and complications of surgery, such as anesthesia, prolonged recovery time, risk of infection, pain, surgical revisions, scars, and bleeding.^{3,13,24} The literature also corroborates the expert panel recommendations that cryolipolysis is appropriate for any skin type and may improve skin tightness by a mechanism in which collagen production is stimulated, new elastin is formed, fibrosis induced, and tissue compacted.^{11,24,31}

The expert panel reached consensus that the "quality" of excess fat is a determining factor in successful outcomes, a recommendation also strongly held by expert clinical opinions expressed in the literature. A number of publications support that fat should be localized (ie, "pinchable," "pockets of fat") for more targeted application and to allow for suctioning in cases where a vacuum-based applicator is used^{24,32,33}; otherwise, longer treatment times and more treatment cycles may be required. As indicated in these Delphi recommendations, cryolipolysis is not indicated for obese patients or patients who have experienced extreme weight change and have diffuse fat areas or flaccid skin to which it is difficult to apply the cryolipolysis device with a precise degree of concentration.^{24,33}

Published data also support the expert panel's recommendations (Table 2) about treatment times, durations between treatments, conditions that make patients appropriate candidates or unsuitable for treatment, and factors that impact patient satisfaction with results, such as

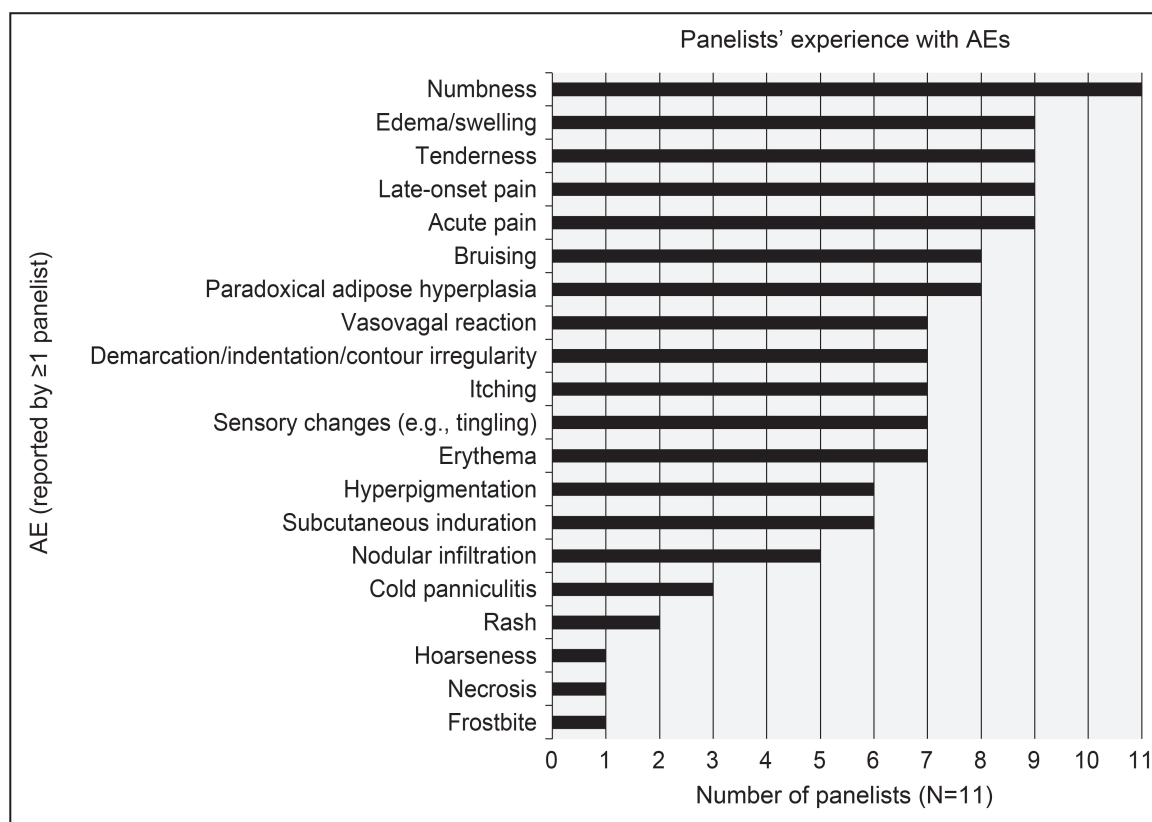


Figure 2. Expert panel experience with cryolipolysis-related AEs. AE, adverse events.

comfort during the procedure.^{24,32,33} Counseling patients on what to expect, eg, improvement in 2 to 3 months, is also recommended in the literature as in these expert consensus recommendations.³²

Recent case reports have drawn attention to PAH as an AE of interest occurring with cryolipolysis.³⁴ Eight of the 11 panelists, or 73%, have encountered PAH in their patients treated with cryolipolysis. In these experts' clinical experience, patients with PAH typically visit plastic surgeons for correction, and PAH may be considered one of the rarer AEs. Nonetheless, the experts reported using the following corrective treatments for PAH: liposuction ($n = 7/8$; 87.5%), deoxycholic acid injection ($n = 2/8$, 25%), thyroxine ($n = 1/8$, 12.5%), surgery ($n = 1/8$, 12.5%), and other temperature-based fat-reduction devices ($n = 2/8$, 25%).

As the number of experts on the Delphi panel was small, the scope of experience with AEs and related clinical intervention strategies may be limited. However, cryolipolysis devices continue to be adapted and developed for greater safety and effectiveness. Authors of a recent study reported that the incident rate for PAH appeared lower in their practice for the newer applicator, CoolAdvantage (ZELTIQ Aesthetics, Allergan Aesthetics, an AbbVie Company, Irvine, CA), compared with legacy applicators.^{35,36} The recommendations produced by this

Delphi process, nonetheless, do not supplant any product labeling, evidence-based treatment guidelines, peer-to-peer training, or clinical judgment.

Future research may be warranted to investigate specific effects of some patient factors, such as gender, age, or skin type, on treatment outcomes, and to explore the number of treatment cycles needed to achieve “treatment to transformation” or “liposuction-like results.”

CONCLUSIONS

Consensus on a number of guideline recommendations associated with cryolipolysis for noninvasive fat reduction was achieved through a modified Delphi method. These recommendations are the first published expert consensus recommendations related to cryolipolysis and may serve as a reference for the broad range of clinicians who perform this noninvasive fat-reduction procedure.

Disclosures

Drs Altmann, Burns, Kilmer, Lee, Lim, Metelitsa, Stevens, Taub, Welsh, and Kazem are advisors for Allergan Aesthetics, an AbbVie Company (Irvine, CA, USA). Dr Welsh is a shareholder of Strasphey-Crown (Newport Beach, CA, USA) and received honoraria from BTL (Boston, MA, USA). Employees of Allergan Aesthetics participated

Table 4. Recommendations for AE Management Strategies and First-line Treatments

Statement	Total panelists (N = 11) selecting <i>strongly agree</i> or <i>agree</i> . n (%)	Strength of consensus ^a	Weighted sum of rating scale responses
Demarcation, indentation, and contour irregularities are variable in nature. Treatment should therefore be dependent on whether the AE consists of a volume deficit or a volume excess.	11 (100)	Complete	1.6
Additional CoolSculpting cycles, liposuction, Kybella (Allergan Aesthetics, an AbbVie Company, Irvine, CA), and radiofrequency-based fat-reduction procedures can be considered viable treatment options when treating contour irregularities with volume excess.	11 (100)	Complete	1.5
While treatment with gabapentinoids is an option for more severe cases of late-onset pain, at-home self-management using clinician-recommended oral pain medication (eg, NSAIDs, acetaminophen) and/or compression will often suffice.	11 (100)	Complete	1.5
It is important to confirm a correct diagnosis of hyperpigmentation before administering treatment, as it can appear similar in nature to posttreatment bruising. Hyperpigmentation does not occur immediately after treatment.	11 (100)	Complete	1.5
Once a patient has been confirmed to have hyperpigmentation as a result of cryolipolysis, clinical action may be needed. Treatments for consideration include bleaching creams (eg, hydroquinone), topical acids (eg, tretinoin, tranexamic acid), or laser therapy.	11 (100)	Complete	1.5
Cold panniculitis as a result of cryolipolysis treatment is rare and is best described as a heightened inflammatory response that can consist of edema, erythematous plaques, and/or nodules.	11 (100)	Complete	1.5
Frostbite, or cold burn, as a result of cryolipolysis treatment is rare, but clinically concerning, and should require an aggressive treatment approach following current treatment guidelines.	11 (100)	Complete	1.6
Necrosis as a result of cryolipolysis treatment is rare, but clinically concerning, and should require an aggressive treatment approach following current treatment guidelines.	11 (100)	Complete	1.6
While fluids, ice packs, and shifting patients into the Trendelenburg position can be used to manage a vasovagal reaction, most important to clinical action is to monitor the patient closely following treatment.	11 (100)	Complete	1.7
Itching as a result of cryolipolysis treatment typically does not require clinical intervention, but diphenhydramine (eg, Benadryl) can be considered an appropriate and helpful form of management.	11(100)	Complete	1.4
PAH resulting from cryolipolysis treatment requires clinical action. Liposuction should be considered the first-line treatment for PAH.	10 (90.9)	Strong	1.6
Hyperpigmentation as a result of cryolipolysis treatment is rare and is typically only seen in patients with skin types 4-6.	10 (90.9)	Strong	1.4
Subcutaneous induration as a result of cryolipolysis treatment typically does not require clinical intervention, but massage may be an appropriate and helpful form of management.	10 (90.9)	Strong	1.3
Prednisone, tranexamic acid, and LED therapy can all be considered treatments for frostbite/cold burn.	8 (72.7)	Moderate	0.8
Prednisone, tranexamic acid, hyperbaric oxygen therapy, and LED therapy can all be considered treatments for necrosis.	8 (72.7)	Moderate	0.9
Fillers can be considered a viable treatment option when treating contour irregularities with volume deficits.	6 (54.5)	No consensus	0.3

^aA moderate consensus rating indicates that 7-8 panelists (63.6% to 72.7%) endorsed a given response, whereas a strong rating indicates that 9-10 panelists (81.8% to 90.9%) endorsed a given response. A complete consensus rating indicates that all 11 panelists endorsed a given response. Consensus was considered not met for recommendations in which 6 or fewer panelists provided endorsement. ^bThe weighted average of panelists' agreement ratings. Sum scores were weighted using the following scaling: strongly agree (2), agree (1), neither agree nor disagree (0), disagree (-1), and strongly disagree (-2). AE, adverse event; LED, light-emitting diode; NSAID, nonsteroidal anti-inflammatory drug; PAH, paradoxical adipose hyperplasia.

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REFERENCES

1. The Aesthetic Society's Cosmetic Surgery National Databank: Statistics 2020. *Aesthet Surg J*. 2020. Accessed March 31, 2021. <https://cdn.surgery.org/media/statistics/aestheticplasticsurgerynationaldatabank-2020stats.pdf>.
2. The Aesthetic Society's Cosmetic Surgery National Data Bank: Statistics 2019. *Aesthet Surg J*. 2019. Accessed October 28, 2020. https://www.surgery.org/sites/default/files/Aesthetic-Society_Stats2019Book_FINAL.pdf.
3. Stevens WG. Response to "Cryolipolysis: The importance of scientific evaluation of a new technique". *Aesthet Surg J*. 2015;35(5):NP120NP120-NP120NP122. doi:10.1093/asj/sju109
4. About CoolSculpting. 2019. Accessed March 18, 2021. <https://www.coolsculpting.com/important-safety-information/>.
5. Avram MM, Harry RS. Cryolipolysis for subcutaneous fat layer reduction. *Lasers Surg Med*. 2009;41(10):703-708. doi:10.1002/lsm.20864
6. Zelickson B, Egbert BM, Preciado J, et al. Cryolipolysis for noninvasive fat cell destruction: initial results from a pig model. *Dermatol Surg*. 2009;35(10):1462-1470. doi:10.1111/j.1524-4725.2009.01259.x
7. Wang S, Ezaldein H, Tripathi R, Merati M, Scott J. An analysis of marketing trends for the approval of cryolipolysis devices by the United States Food and Drug Administration. *J Clin Aesthet Dermatol*. 2019;12(7):59-60.
8. Jalian HR, Avram MM. Body contouring: the skinny on noninvasive fat removal. *Semin Cutan Med Surg*. 2012;31(2):121-125. doi:10.1016/j.sder.2012.02.004
9. Ortiz AE, Avram MM. Noninvasive body contouring: cryolipolysis and ultrasound. *Semin Cutan Med Surg*. 2015;34(3):129-133. doi:10.12788/j.sder.2015.0171
10. Adjadj L, SidAhmed-Mezi M, Mondoloni M, Meningaud JP, Hersant B. Assessment of the efficacy of cryolipolysis on saddlebags: a prospective study of 53 patients. *Plast Reconstr Surg*. 2017;140(1):50-57. doi:10.1097/PRS.0000000000003433
11. Stevens WG. Does cryolipolysis lead to skin tightening? A first report of cryodermadstringo. *Aesthet Surg J*. 2014;34(6):Np32-Np34.
12. Krueger N, Mai SV, Luebberding S, Sadick NS. Cryolipolysis for noninvasive body contouring: clinical efficacy and patient satisfaction. *Clin Cosmet Investig Dermatol*. 2014;7:201-205. doi:10.2147/CCID.S44371
13. Garibyan L, Sipprell WH, 3rd, Jalian HR, Sakamoto FH, Avram M, Anderson RR. Three-dimensional volumetric quantification of fat loss following cryolipolysis. *Lasers Surg Med*. 2014;46(2):75-80. doi:10.1002/lsm.22207
14. Lim T, Ding SW, Chua CH, Moey HX. Enhancing the appearance of the "six-pack" muscles using cryolipolysis: a safe and effective method. *Plast Reconstr Surg*. 2021;148(4):775-779.
15. US Food and Drug Administration. Zeltiq device classification flanks. 2010. Accessed September 16, 2019. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?ID=DEN090002>.
16. *CoolSculpting System User Manual*. Zeltiq Aesthetics, Inc.; 2018.
17. Harper M, Lassetter J. Coolsculpting or cryolipolysis, a guide for primary care providers. Paper 264. 2019. Accessed March 17, 2021. <https://scholarsarchive.byu.edu/studentpub/264/>.
18. Harper M, Lassetter J. CoolSculpting or cryolipolysis: a guide for primary care practitioners. Paper 265. 2019. Accessed March 17, 2021. <https://scholarsarchive.byu.edu/studentpub/265/>.
19. McKeown DJ, Payne J. Significant improvement in body contour with multiple cycles of CoolSculpting: results of a prospective study. *Dermatol Ther*. 2021:e14850.
20. Rosario N, Kemp J, Mushtaq Y, Boter M. *Cool-sculpting: optimizing total fat loss during cryolipolysis*. 2018. Accessed March 17, 2021. <https://ecommons.cornell.edu/handle/1813/57227>.
21. Derrick CD, Shridharani SM, Broyles JM. The safety and efficacy of cryolipolysis: a systematic review of available literature. *Aesthet Surg J*. 2015;35(7):830-836. doi:10.1093/asj/sjv039
22. Bernstein EF. Long-term efficacy follow-up on two cryolipolysis case studies: 6 and 9 years post-treatment. *J Cosmet Dermatol*. 2016;15(4):561-564. doi:10.1111/jocd.12238
23. Swanson E. Cryolipolysis: the importance of scientific evaluation of a new technique. *Aesthet Surg J*. 2015;35(5):NP116NP116-NP116NP119. doi:10.1093/asj/sju069
24. Meyer PF, Davi Costa ESJ, Santos de Vasconcellos L, de Moraes Carreiro E, Valentim da Silva RM. Cryolipolysis: patient selection and special considerations. *Clin Cosmet Investig Dermatol*. 2018;11:499-503.
25. Jain M, Savage NE, Spiteri K, Snell BJ. A 3-dimensional quantitative analysis of volume loss following submental cryolipolysis. *Aesthet Surg J*. 2020;40(2):123-132. doi:10.1093/asj/sjz145
26. Hedayati B, Juhász M, Chu S, Mesinkovska NA. Adverse events associated with cryolipolysis: a systematic review of the literature. *Dermatol Surg*. 2020;46(Suppl 1):S8-S13.
27. Hsu C-C, Sandford BA. The Delphi technique: making sense of consensus. *Practical Assess Res Eval*. 2007;12(12).
28. Stroumza N, Gauthier N, Senet P, Moguelet P, Nail Barthelemy R, Atlan M. Paradoxical adipose hypertrophy (PAH) after cryolipolysis. *Aesthet Surg J*. 2018;38(4):411-417. doi:10.1093/asj/sjx159
29. Benoit C, Modarressi A. Severe frostbite complication after cryolipolysis: a case report. *JPRAS Open*. 2020;25:46-51. doi:10.1016/j.jpra.2020.05.004

30. Nseir I, Lievain L, Benazech D, Carricaburu A, Rossi B, Auquit-Aukbur I. Skin necrosis of the thigh after a cryolipolysis session: a case report. *Aesthet Surg J*. 2018;38(4):Np73-Np75.
31. Stevens WG, Gould DJ, Pham LD, Jimenez Lozano JN. Molecular and histological evidence detailing clinically observed skin improvement following cryolipolysis. *Aesthet Surg J*. 2022;42(1):56-67. doi:10.1093/asj/sjab226
32. Stevens WG, Bachelor EP. Cryolipolysis conformable-surface applicator for nonsurgical fat reduction in lateral thighs. *Aesthet Surg J*. 2015;35(1):66-71. doi:10.1093/asj/sju024
33. Lewis J. Cryolipolysis is an effective treatment modality for non-invasive body sculpting. *J Aesthet Nurs*. 2016;5(7):337-338.
34. Agochukwu-Nwubah N, Mentz H. Paradoxical adipose hyperplasia after noninvasive radiofrequency treatment: a novel report and review. *J Cosmet Dermatol*. 2020;19(4):866-868. doi:10.1111/jocd.13090
35. Nikolis A, Enright KM. A multicenter evaluation of paradoxical adipose hyperplasia following cryolipolysis for fat reduction and body contouring: a review of 8,658 cycles in 2,114 patients. *Aesthet Surg J*. 2021;41(8):932-941. doi:10.1093/asj/sjaa310
36. *CoolSculpting Elite System User Manual*. Zeltiq Aesthetics, Inc.; 2020.