



A Clinical Guide to the Treatment of Cellulite and Comprehensive Review of the Etiology, Pathophysiology, and Utility of Intervention



Ambika Menon¹ · Orr Shauly² · Troy Marxen² · Albert Losken² · Heather R. Faulkner²

Received: 5 August 2023 / Accepted: 14 November 2023 / Published online: 6 December 2023

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Abstract

Introduction Cellulite is a common esthetic concern affecting most women. Despite its prevalence, there is no consensus on the optimal treatment approach for cellulite, partly due to the complex and multifactorial nature of its pathophysiology. Understanding the underlying biological processes along with available treatment options is important to be able to effectively counsel patients on effective management of this condition. This review aims to focus on high-quality evidence behind pathophysiology of cellulite, severity and grading, and its available treatment options.

Methods A comprehensive review of the literature was performed using PubMed and Embase databases. Manuscripts that provided objective data with respect to pathophysiology, grading scales, and applications of treatment options were utilized.

Results Using the existing CSS classification, an evidence-based algorithm is proposed for treatment of cellulite. Mild cellulite is best served with lifestyle modifications such as healthy diet, hydration, and exercise. Use of topicals in mild cellulite patients as adjuncts to lifestyle modifications have the highest efficacy, although there are inconsistent data on topical treatments. Moderate cellulite is best targeted with noninvasive treatment options including laser therapy, radiofrequency, and ultrasound. Radiofrequency demonstrates the strongest efficacy in the current peer-reviewed literature. Severe cellulite is recommended to be

treated with minimally invasive approaches such as subcision and injectables.

Conclusion Cellulite is a challenging cosmetic problem to treat, and thus multimodal treatment options should be considered in an attempt to achieve optimal outcomes and patient satisfaction. As the pathophysiology of cellulite is further elucidated, more targeted treatments may be developed in the future.

Level of Evidence V This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Cellulite · Cellulite treatment · Cellulite review · Microneedling cellulite · Pathophysiology · Cellulite etiology · Cellulite laser-therapy · Cellulite ultrasound

Introduction

Cellulite, a common esthetic concern affecting the skin and subcutaneous tissue, has been reported to affect up to 90% of post-pubertal females. This topic has been a subject of interest among researchers and clinicians for many years [1]. Despite its high prevalence, there is no consensus on the optimal treatment approach for cellulite, partly due to the complex and multifactorial nature of its pathophysiology. Understanding the underlying biological processes along with available treatment options is important to be able to effectively counsel patients on effective management of this condition.

There is a paucity of peer-reviewed literature supporting an evidence-based approach to cellulite treatment. Many

✉ Orr Shauly
orr.shauly@gmail.com

¹ Emory University School of Medicine, Atlanta, Georgia

² Division of Plastic and Reconstructive Surgery, Emory University School of Medicine, Atlanta, Georgia

studies on cellulite interventions are qualitative due to differences in severity scales, with small sample sizes, lack of standardized outcome measures, and limited randomized controlled trials [2, 3]. This dearth of high-quality evidence makes it challenging to establish consistent guidelines for cellulite management, resulting in variability in treatment approaches and outcomes in clinical practice.

We aim to provide a comprehensive review of the pathophysiology of cellulite, including the structural changes in the skin and connective tissue, alterations of adipose tissue, hormonal and genetic influences, and inflammatory processes that may be present. We have critically evaluated existing treatment options, including both noninvasive and invasive interventions to guide clinical decision making. We additionally aim to develop an algorithm for the treatment of cellulite. The overarching goal is to contribute to the understanding of the pathophysiology of cellulite and provide evidence-based recommendations for treatment selection.

Pathophysiology

The pathophysiology of cellulite is complex and multifactorial. It involves the accumulation of subcutaneous adipose, changes in connective tissue structure, and alterations in microcirculation [4–6]. Adipocytes in affected areas become enlarged, causing compression of blood vessels and lymphatic vessels, leading to impaired blood flow and lymphatic drainage [4, 6]. Fibrous septae encircling the adipocytes lose compliance, causing the adipocytes to become compressed and subsequently protuberant, which create the characteristic dimples on the skin surface commonly referred to as cellulite [4, 7]. Hormonal factors, genetic predisposition, poor circulation, inflammation, and lifestyle factors such as diet and lack of exercise are believed to contribute to the development of cellulite [1, 8, 9]. It is primarily found in the gluteal-femoral regions, but can also be found in other areas such as the trunk and upper extremities [1, 4, 8, 9]. Although often associated with obesity, excess adipose tissue can worsen the condition, but is not specific to the development or pathogenesis of cellulite [4, 7].

Classification

Cellulite currently has multiple classification scales, with some proposing only qualitative measures, and there is no one main validated scale [7]. The oldest, most-cited classification system is the Nürnberger–Müller (Table 1) which categorizes cellulite into four grades (0–III) [4, 7, 8]. Another frequently cited classification system is the Cellulite Severity Scale (CSS) (Table 2), which was developed to include specific morphological and clinical aspects of

cellulite, thereby providing a more clinically accurate picture of severity, although validated only for the thigh and buttocks [7]. This scale grades cellulite severity on 5 criteria—number of evident depressions, depth of depressions, morphological appearance of skin surface alterations, grade of laxity, flaccidity or sagging skin, and the classification by Nürnberger–Müller, thereby giving each patient a score between 1 and 15 [7, 10]. A score of 1–4 is categorized as mild, 5–10 is moderate, and 11–15 is severe [10]. While these classifications exist, they do not accurately direct the clinician to specific methods of treatment, which would be a useful addition to inform patient care for this condition [7].

Etiology

While much about the etiology of cellulite remains unclear, there are predisposing risk factors that may contribute to an increased risk of developing the condition. Hormonal changes during pregnancy, menopause, and hormonal imbalances such as polycystic ovarian syndrome (PCOS) can increase the risk of developing cellulite due to the influence of estrogen and progesterone on the connective tissue structure and fat distribution [5, 8]. Hyperestrogenism has been implicated in the formation of cellulite and thus is rarely seen in men without androgen deficiencies [1, 11]. While the pathophysiology is not entirely elucidated, high levels of estrogen are said to rearrange fatty tissues, through the stimulation of fibroblasts which degrade collagen fibers leading to the characteristic phenotype of cellulite [11, 12]. Lifestyle factors, such as lack of exercise, poor dietary habits, and moderate to high alcohol intake, can worsen cellulite [8]. Lack of physical activity and a diet high in processed foods, saturated fats, and sugars can lead to weight gain, fat accumulation, and decreased muscle tone, which can all contribute to the formation and exacerbation of cellulite [1, 8]. Genetic predisposition may also increase patient risk of cellulite development. Family history of cellulite was identified as a risk factor in 1 study, with patients having an increased incidence due to potential genetic factors that influence connective tissue structure, fat metabolism, and inflammation [1, 13]. At the present time, etiology does not dictate treatment, and therefore treatment is based on severity.

Treatment Options

Topical

Topical treatments are often used as part of a multimodal approach to cellulite treatment, although long-term efficacy

Table 1 Nürnberger–Müller cellulite staging (a component of the Cellulite Severity Scale)

Stage	Phenotypic description
Stage 0	No alteration of skin topography. The skin remains smooth while standing or lying.
Stage I	The skin around the affected area is smooth while standing or lying. Changes, including “mattress appearance” can be seen while pinching the skin.
Stage II	The skin is smooth while lying, but alterations, including “mattress appearance” are observed while standing.
Stage III	Skin has a “mattress appearance” while sitting and standing.

Table 2 Cellulite Severity Scale components and scoring

Score	Total visible depressions	Depression depth	Morphologic appearance	Laxity	Nürnberger–Müller classification
0	None: no depressions.	No depressions	No raised areas.	Absence of laxity, flaccidity, or sagging skin.	Zero grade
1	A small amount: 1–4 depressions are visible.	Superficial Depressions	Orange peel’ appearance.	Slight draped appearance.	First grade
2	A moderate amount: 5–9 depressions are visible.	Medium Depth Depressions	“Cottage cheese” appearance.	Moderate draped appearance.	Second grade
3	A large amount: 10 or more depressions are visible.	Deep depressions	“Mattress” appearance.	Severe draped appearance.	Third grade

is uncertain. Some topical substances contain ingredients such as caffeine, retinol, or herbal extracts that claim to improve the appearance of cellulite by reducing fat accumulation, increasing circulation, or improving skin texture [3, 5, 14]. Methylxanthines, such as caffeine or theophylline, have been effective in transiently reducing the physical manifestations of cellulite by inducing lipolysis through the inhibition of phosphodiesterase activity and their action as antioxidants [3, 5, 14]. Retinoic acid and vitamin A derivatives have similarly been implicated in improving the appearance of cellulite through increasing fibroblast proliferation, improving collagen thickness and inhibiting differentiation of adipocyte precursors [4, 14]. However, the evidence on the effectiveness of topicals in cellulite treatment has found that the effects are transient in helping the appearance of cellulite. This is because topical substances do not penetrate the skin to affect the fibrous septa which create the peau d’orange manifestation on the skin [14]. In general, there is minimal risk to the use of most topical agents [14]. Therefore, it is up to the plastic surgeon to determine whether they wish to include topical treatments as part of a cellulite treatment regimen.

Radiofrequency

Radiofrequency (RF) treatment is a noninvasive or minimally invasive option that is commonly used in the

treatment of cellulite [15–22]. The RF waves penetrate the skin and generate heat in the subcutaneous adipose layer, which stimulates collagen production, improves blood circulation, and promotes lymphatic drainage. The two primary modalities of devices utilized in RF are unipolar and bipolar. They are differentiated by the depth that the RF waves reach, with unipolar reaching deeper layers than bipolar [14]. RF has also been proposed as a method to improve the appearance of cellulite by specifically targeting and tightening the superficial fascial system such as the fibrous septae and adipose tissue implicated in the formation of cellulite [15]. While noninvasive and effective, much like topicals, the effects are typically temporary, requiring maintenance appointments as well as variable results depending on skin type, cellulite severity, and treatment settings [2, 23]. RF microneedling has seen improvements in collagen formation and skin texture for up to 6 months post-treatment, indicating that there may be longevity to treatment effects [24]. RF is primarily utilized as an adjunct to other techniques including liposuction or ultrasound due to its controversial level of efficacy alone [14, 25].

Laser

Laser treatment is another popular non-surgical approach for the treatment of cellulite. Laser devices utilize various

wavelengths of light to target fat cells, stimulate collagen production, and improve skin tightness [5, 25]. Some studies have reported positive results with laser treatment in reducing cellulite severity and improving the overall appearance of the skin affected by cellulite (1440-nm Nd:YAG laser) [25]. Similar to RF, laser is noninvasive and effective; however, the effects are typically temporary, requiring maintenance appointments as well as variable results depending on skin type, laser type, cellulite severity, and treatment settings. Treatments have been found to have variable longevity, with some studies demonstrating maintenance of results within a broad range of 6 weeks to 3 years post-treatment [26, 27]. These studies employed different treatment frequency, with some twice per week for a 3-week period, and others a single treatment with majority of the patients being Fitzpatrick II or III and CSS of 2–3 [26, 27]. The great variation in outcomes indicates a significant need for continued research in the efficacy of laser in a diverse spectrum of Fitzpatrick skin types and cellulite severities.

Acoustic Wave Therapy

Acoustic wave treatment, also known as extracorporeal shockwave therapy (ESWT), is a noninvasive approach used in the treatment of cellulite. This treatment uses high-energy acoustic waves to target and disrupt the fibrous bands that contribute to cellulite formation, aiming to improve blood flow, stimulate collagen production, and reduce the appearance of cellulite [25]. Two forms of ESWT are available: radial and focused. Radial systems produce dispersed energy which create a diffuse and superficial effect on tissues [5]. Focused systems are higher energy and penetrate into deeper layers of tissue [5]. While most studies looking at outcomes post-ESWT have targeted the buttocks and the outer and inner thighs, all have reported significant improvement in reducing cellulite

severity and improving skin texture, following radial and focused ESWT (Table 3) [28–30]. Allam et al. investigated the effect of ESWT as an adjunct therapy after 1 session of liposuction and found that it was significantly more effective than manual lymphatic drainage in maintaining effects of liposuction and continued reduction of cellulite severity [31].

Subcision

Subcision is a minimally invasive surgical technique that has been used for the treatment of cellulite. Manual subcision involves the release of fibrous bands that contribute to the appearance of cellulite, aiming to smooth out the skin surface. This is performed with insertion of a needle, such as an 18-gauge non-coring needle, or forked cannula beneath the skin around 10–20 millimeters into the subcutaneous adipose tissue layer, parallel to the skin [33]. By severing the fibrous septae, there is a redistribution of subcutaneous forces which in turn reduces adipose lobule extrusion and ultimately the physical manifestations of cellulite [33]. Depth of the needle or cannula is paramount to the success of the procedure: If too superficial, necrosis of skin or elevation of skin can occur; if too deep, disruption of surrounding structures and incomplete correction can result [33]. Studies have reported positive results with subcision in reducing the severity of cellulite and improving the overall contour of the skin in a single treatment [14, 34]. Targeted verifiable subcision (TVS) devices (Avéli, Westlake Dermatology®) utilize minimally invasive mechanisms through small incisions to allow for fibrous septae release across multiple septae [9]. This device has a deployable hook which allows you to track progress through subcutaneous fat layer and then have tactile and visual feedback through engagement with septa and visualized release of bands despite multiple orientations and across multiple septae [9]. The minimization of

Table 3 Summary of outcomes of acoustic wave therapy in the treatment of cellulite

Study	Technique	Treatment length	Esthetic target	Outcomes
Hessel et al. [28]	Acoustic wave therapy (AWT)	12 sessions over 6 weeks	Gluteus and posterior thighs	Reduction in circumference of thighs and visibility of cellulite.
Adatto et al. [32]	Radial and planar AWT	8 sessions in 4 weeks	Thighs	Reduction in circumference of thighs and subcutaneous fat layer thickness.
Nassar et al. [30]	Radial and planar AWT	8 sessions in 4 weeks	Lateral thighs	No significant change in circumference or visibility.
Knobloch et al. [29]	Focused AWT	6 sessions over 12 weeks	Gluteal and thigh regions	Improvement in cellulite severity in patients with moderate-to-severe cellulite.
Allam et al. [31]	AWT	Two sessions per week for four weeks	Anterior thighs	Significant decrease in cellulite grading scale in patients with grade three cellulite.

cellulite through a single session of TVS has been demonstrated through one year, with strengths of visualization and tactile feedback not experienced through standard subcision techniques [9].

Injectables

Injectables, such as dermal fillers or fat-dissolving agents, have been explored as a potential treatment option for cellulite. Injectables are now comprised of diverse options including collagenases, hyaluronidase, lipases, and aminophylline [14]. While each injectable maintains its own mechanism of utility, dermal fillers can be used to add volume and improve the smoothness of the skin affected by cellulite, while fat-dissolving agents aim to target and reduce excess fat deposits associated with cellulite [1]. Use of collagenase clostridium histolyticum (CCH-aaes) injectables (Qwo, Endo Aesthetics →) has been found to be effective in the treatment of moderate-to-severe cellulite in the buttocks and thighs (Table 4) [35, 36]. The mechanism of action of CCH-aaes is twofold: It lyses septae and stimulates neocollagenesis in subcutaneous fat into more compact and homogenous fat lobules [37]. In fact, in a study looking at five different injection techniques of CCH-aaes in the thigh and buttocks, all were equally efficacious when using the product despite needle angle, volume of product, and depth of injection [37].

Discussion

There are a variety of available treatments for the common cosmetic concern of cellulite. However, there is no clear algorithm for how best to treat it due to the lack of standardization of a grading scale, a paucity of randomized

controlled trials exploring efficacy of different treatments, and a pathophysiology that has yet to fully be elucidated. There are currently noninvasive and minimally invasive treatments available, and treatments are not based on etiology.

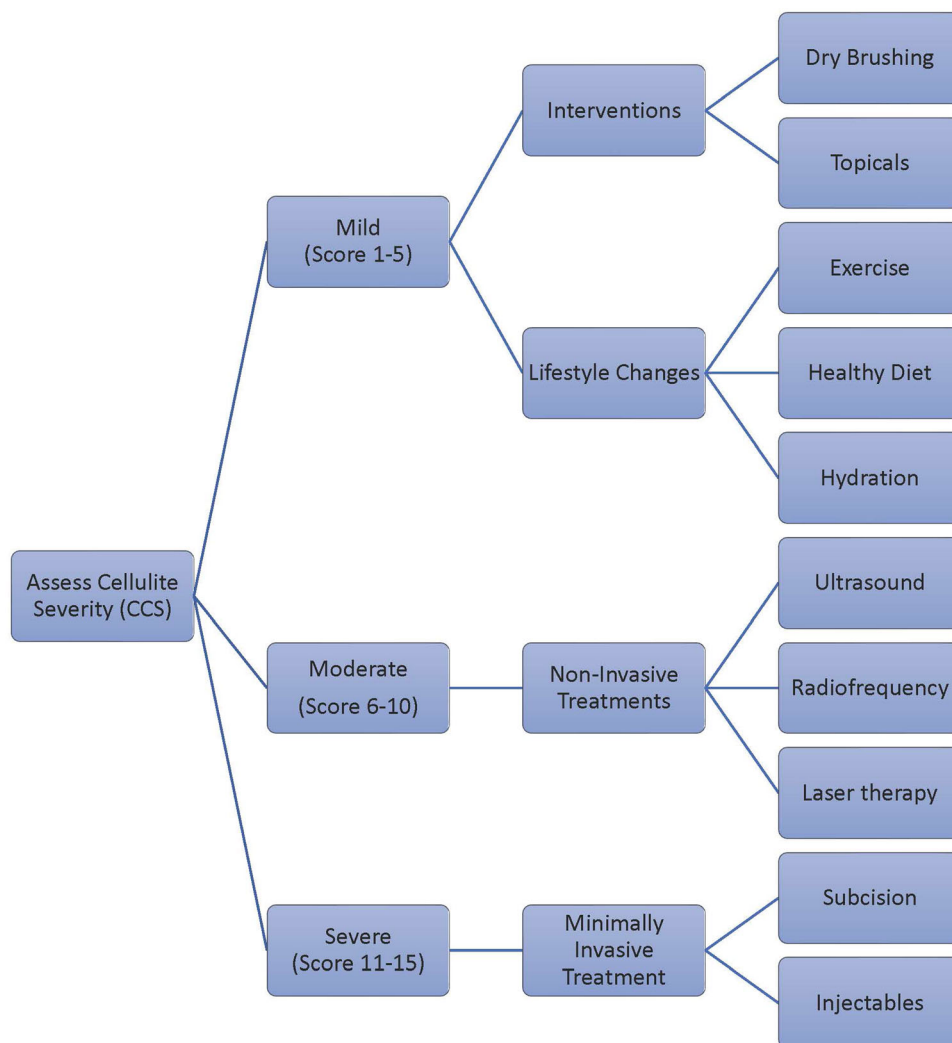
Using the existing CSS classification, we propose an evidence-based algorithm for treatment (Figure 1). Mild cellulite (score 1–5) is best served with lifestyle modifications such as healthy diet, hydration, and exercise. The low risk and transient benefits of topicals in mild cellulite patients are adjuncts to lifestyle modifications that have the highest efficacy in this patient population, although there are inconsistent data on topical treatments. Moderate cellulite (score 6–10) is best targeted with noninvasive treatment options including laser therapy, radiofrequency and ultrasound. Radiofrequency demonstrates the strongest efficacy in the current peer-reviewed literature; however, a stepwise multimodal approach is still recommended with these patients, with a trial of noninvasive options with a 3–4-week waiting period between treatments to assess clinical improvement. Severe cellulite (score 11–15) is recommended to be treated with minimally invasive approaches such as subcision and injectables; however, the evidence for these treatments is still weak.

Cellulite is a common cosmetic concern affecting many individuals, particularly women. While various treatment options exist, the efficacy of each option may vary depending on the severity of cellulite and patient characteristics. Utilizing a multimodal approach in cellulite treatment may provide more comprehensive results by combining different treatments to target different aspects of the condition. Plastic surgeons are uniquely positioned to offer a variety of treatment options to their patients, and by utilizing multimodal treatment and the algorithm outlined in this manuscript, they can optimize results and improve

Table 4 Summary of outcomes of injectables in the treatment of cellulite

Injectable Type	Studies cited	Esthetic target	Outcomes
Clostridium histolyticum	Yang et al. [38], Sadick [2], Graivier et al. [35], Joseph et al. [36], Kaufman-Janette et al. [37].	Thighs, buttocks	Effective for treatment of moderate-to-severe cellulite.
Calcium hydroxyapatite	Lapatina et al. [39]	Thigh, buttocks	Improved skin elasticity and increased skin tightening in the upper arms and abdomen after only a single treatment, while stimulating collagen production.
Poly-L-lactic acid	Christen et al. [40] Perez Atamoros et al. [14]	Neck, chest, buttocks, thigh, abdomen, arms	Tightening of skin and reduction of cellulite severity.
Hyaluronidase	Da Silva [41], Perez Atamoros et al. [14]	Abdomen, thighs, gluteus	Reduction in cellulite visibility and severity.
Sodium deoxycholate	Rotunda et al. [42], Galadiri et al. [43] Perez Atamoros et al. [14]	Thighs, gluteus	Targets fatty deposits in the subcutaneous tissue and induces lipolysis, reducing visibility of cellulite.

Fig. 1 Algorithm for treatment of cellulite



patient satisfaction. Future research is needed to determine the most effective combination of treatments for cellulite and to identify factors that may influence treatment outcomes and long-term efficacy.

Conclusion

Cellulite is a challenging cosmetic problem to treat. Consideration should be given to multimodal treatment options in an attempt to achieve optimal outcomes and patient satisfaction. As the pathophysiology and underlying cause of cellulite is further elucidated, more targeted treatments may be developed in the future. The use of a consistent and objective assessment tool when evaluating patients with cellulite may assist in standardizing treatment. More research is needed to understand the formation of cellulite with the hope of improving treatment.

Funding None.

Declarations

Conflict of interest The authors declare that they have no conflicts of interest to disclose.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent For this type of study, informed consent is not required.

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