

## Lipodystrophy: A Literature Review

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### Summary

*Gynoid lipodystrophy (GLD), also known as edematous adiposity and deforming dermatopaniculosis and commonly called cellulite, occurs as a result of fat deposition under the skin. It is characterized by structural, inflammatory, and biochemical disorders of the subcutaneous tissue that cause irregular changes in the appearance of the epidermis. These consist of bulges caused by projections of fat and subcutaneous structures towards the skin's surface, together with depressions caused by skin retraction due to subcutaneous fibrous septa. The female population accounts for 95% of gynoid lipodystrophy cases where it usually appears after puberty. It is potentially exacerbated during periods of increased estrogen levels such as pregnancy, breastfeeding, menstruation, and the use of oral contraceptives [1,2,3,4].*

**Keywords:** gynoid lipodystrophy, cellulite, treatments, aesthetics.

### Introduction

Gynoid lipodystrophy (GLD) is a complex and multifactorial condition, and there is still much uncertainty about its causes and/or predispositions. Theories attempt to explain its onset, but to date nothing has been conclusively proven. The literature suggests that gynoid lipodystrophy can be influenced by triggering, perpetuating, and exacerbating factors such as stress, sedentary lifestyle, obesity, heredity, age, sex, hormonal dysfunctions, smoking, pregnancy, excessive caffeine and alcohol consumption, inadequate nutrition, mechanical factors, anatomical alterations, microcirculation failure, reduced production of the vasodilator hormone adiponectin by subcutaneous cellular tissue, genetic polymorphism, alterations in dermal connective tissue, inflammatory processes, and the use of hormonal contraceptives [1,2,5,6].

Theories suggest that GLD is chronic edema of the connective tissue due to water accumulation and fibrosis of the affected region; others theories suggest it results from an alteration in microcirculation characterized by compression of the venous and lymphatic systems; and still others focus on the perpendicular orientation of the interlobular septa in subcutaneous tissue since it has been observed in MRIs that female GLD patients present more perpendicular septa when compared to male patients or patients who do not have GLD [7].

That GLD affects more women than men could be attributed to either the direction of collagen fibers or the presence of estrogen. Some authors note that estrogen plays a fundamental role in the pathophysiology of GLD because it can inhibit lipolysis and increase lipogenesis, resulting in hypertrophy of adipose tissue. Estrogen also influences the permeability of blood vessel walls and can consequently lead to edema of the surrounding tissues and thus compression of the circulatory system [5,6,7].

Increased estrogen levels are associated with exacerbation of GLD (glomerular lipodystrophy), and therefore pregnant women, breastfeeding women, those on their menstrual period, or those using oral contraceptives may experience increased lipodystrophy [5,7].

MRI has proven important in studying the pathophysiology of GLD where it has shown a significant increase in the presence and thickness of underlying subcutaneous fibrous septa which cause visible skin depressions and irregularities. Physiologically, fibrous septa can be found oriented between 45° to perpendicular to the skin surface; however, it has been observed that female patients with GLD have significantly more thin and perpendicular septa which maintain downward tension perpendicular to the skin surface and result in visible skin depressions [2,7].

### Pathophysiology

Located in the hypodermis, adipocytes are the cells responsible for storing dietary fat as an energy reserve. Arteries, veins, and the lymphatic system circulate between these cells, supplying them with blood, oxygen, and nutrients, as well as transporting metabolic waste products back into circulation. Adipose tissue also contains collagen fibers that separate groups of adipocytes [8,9].

With an increase in deposited fat, adipocytes increase in size and compress the circulatory system which results in changes in the distribution of blood, oxygen, and nutrients to the cells. This compression also alters the return of metabolic waste products to circulation. This causes edema, which further accelerates the formation of cellulite. When women experience an increase in deposited fat, the thin, perpendicular collagen fibers are put under increased tension and potentially cause skin depressions and irregularities. In men, however, these fibers are thicker and can more easily resist surface deformation with fat

accumulation, thus leaving a smooth and normal skin appearance [8,9].

In addition to adipocytes, adipose tissue is also composed of pre-adipocytes, fibroblasts, leukocytes, macrophages, endothelial cells, and myocytes. So, while the main function of adipose tissue is to store and metabolize fatty acids, it also impacts endocrine activity and plays a complex role in the body's overall functioning. Therefore, when there is an alteration in this tissue, not only will the appearance of the skin be altered but metabolism as well. It can be concluded, then, that GLD (glomerular lipodystrophy) may not be considered merely an aesthetic disorder, but also a homeostatic disorder [5].

While GLD is not obesity (a disease caused by the accumulation of fat in the body), it may be associated with the onset of this condition. Both obesity and gynoid lipodystrophy are affected by a lifestyle including poor diet and sedentary behavior [5,7].

Excessive consumption of high-fat, processed foods that are high in sodium and preservatives are associated with the onset of lipodystrophy. This consumption pattern can also lead to hyperinsulinemia which is another trigger for the condition. An imbalanced diet and sedentary lifestyle increases the severity of lipodystrophy as the muscle layer weakens and potentially causes homeostatic disturbances in blood vessels that lead to hypoxia and ischemia of adipose tissue. Other important factors related to the clinical progression of lipodystrophy include alcohol consumption, which stimulates lipogenesis and causes dehydration resulting in excessive and inappropriate fat storage, and tobacco use, which results in higher amounts of free radicals (and which, in excess, can be toxic and harmful to health) and stimulates the contraction of blood vessels, causing microcirculatory disorders [5,7].

### Classification

Researchers are constantly searching for the best methods to classify degrees of gynoid lipodystrophy in ways that account for a patient's quality of life with a view to providing the best treatment and ways of monitoring results.

In 1978, Nurnberger and Muller offered the first GLD classification described in the literature. The clinical aspects of visible irregularities were used as data points, resulting in the 4 degrees described below [6,10].

Zero: no changes in the skin surface;

I: visible changes in skin pinching or muscle contraction;

II: visible changes when there is no manipulation;

III: Visible changes associated with nodules.

This classification raises questions because it relies on qualitative information that is subject to broad interpretation and therefore casts doubt on its comparative therapeutic efficacy before and after treatments [3].

A new methodology has been proposed to classify cellulite more objectively using a numerical scale based on more extensive clinical and visual assessments. The Cellulite Severity Scale (CSS) rates 5 variables, the sum of which results in 3 categories [3,4].

### The five examined variables:

A- Number of visible depressions;

B- Depth of visible depressions;

C- Morphological appearance of skin surface changes;

D- Degree of skin laxity or looseness;

E- Nuremberg and Müller scale classification.

**Points from 0 to 3 are assigned to these, resulting in a final sum of between 0 and 15 that classifies a patient into 3 categories:**

Light (1-5 points);

Moderate (6-10 points);

Severe (11-15 points).

In clinical practice, many physicians still use the Nurnberger and Muller classification due to its ease of application. However, in scientific articles and studies, the CSS is recommended for a better standard of comparison. The Brazilian Society of Dermatology classifies GLD (glomerular lymphoma) grades according to the CSS [11].

### Treatments

There are several treatment options for gynoid lipodystrophy and they all involve changes in a patient's habits, including improved diet, increased water intake, and regular physical activity. Because GLD is a multifactorial condition, there is still no simple and definitive treatment, and further studies in the area are needed [2,3,6].

Treatments for GLD can be classified as invasive and non-invasive, and can be combined in a treatment protocol specific to each patient that aims to improve the appearance of the skin [2,3].

All treatments are performed after individual assessment, require a signed consent form, and include pre- and post-procedure guidance.

#### • Non-invasive

**Topical:** Topical therapies serve as adjuncts in the treatment of GLD. On their own, they are not effective as they have only a transient effect and do not act on the skin depressions caused by the fibrous septa. Numerous active ingredients are used in topical formulations to treat GLD, and most contain caffeine, retinol, or botanical derivatives. The adjuvant effects of these products include stimulation of peripheral microcirculation, promotion of lipolysis, increased dermal neocollagenesis, lymphatic drainage, and reduction of edema [2,3,7].

**Oral:** Oral therapies themselves have always been dubious; however, like topical therapies, they can act as an adjunct in the treatment of GLD. Currently, and especially in cases of associated lipedema, oral therapies have gained prominence to become a key component in satisfactory outcomes. They primarily act as nutritional supplements, potentially acting as antioxidants, as stimulators of cellular metabolism and of collagen and elastin synthesis, and as reducers of edema and inflammation [2,12].

**Massage/Endermology:** Developed by Emil and Estrid Vodder in 1936, lymphatic drainage is a technique that aids in the body's lymphatic circulation by draining fluids that accumulate in interstitial spaces and thus contributing to tissue water balance. However, like topical therapies, its effects are temporary. The main purpose of massage is to reduce lymphedema associated with lymph node dissection (LDD) by promoting lymphatic drainage and microcirculation in the subcutaneous tissue. This technique can be performed manually (massage) or with the aid of devices for greater consistency and speed (endermology) [2,3,6,7]

**Cryolipolysis:** This technology causes the controlled freezing of subcutaneous tissues with the aim of reducing fat volume. This technique was approved by the Food and Drug

Administration (FDA) in 2010 for thigh, flank and abdominal fat and in 2014. Its use in the treatment of GLD is limited to the reduction of local fat and does not affect the fibrous septa [2,13]

**Ultrasound:** This technique has become an adjunct treatment for GLD. It works by converting mechanical ultrasonic wave stimulation into thermal energy, altering the structural integrity of tissues and leading to the rupture of adipocyte cell walls. Ultrasound is usually used in conjunction with other treatments for GLD because alone it achieves limited results [2].

**Infrared light and intense pulsed light:** Infrared light utilizes the heat generated in the skin to improve blood and lymphatic microcirculation and to stimulate collagen production [2]

Known as IPL, intense pulsed light uses limited dermal damage to stimulate the repair, productions and remodeling of collagen to result in firmer and more homogeneous dermis with an improved aesthetic appearance [2,3] The limited depth of these exclusively cutaneous treatments provides results that are neither significant nor long-lasting for GLD.

**Radiofrequency:** Approved by the FDA for clinical use in 2006, radiofrequency devices generate heat in the dermis and subcutaneous tissue using resistance to electric current. By affecting septal and adipose connective tissue, this therapy reduces the appearance of cellulite. It is usually combined with other cellulite treatments because of its limited affects when use alone [2,14].

- **Minimally Invasive**

**Carboxytherapy:** Described by Brandi, carboxytherapy is a non-surgical technique in which carbon dioxide (CO<sub>2</sub>) is administered intradermally to induce hypercapnia (increased CO<sub>2</sub> in arterial blood) and thus reduce local pH. This technique aids in the treatment of GLD by improving blood and lymphatic flow, restoring elasticity and neutralizing flaccidity, reducing fat deposits, and improving blood microcirculation [2,3].

**Mesotherapy:** Discovered by Dr. Michel Pistorin 1958 and recognized by the French National Academy of Medicine in 1987, mesotherapy is still used today in various sectors. The technique involves intradermal therapy, or the subcutaneous injection of compounds. Several methodologies can be used, and the active ingredients and compounds vary according to symptoms [2,3,15]

**Subcutaneous Incisionless (Subcision) Surgery:** first described in 1995, this is a minimally invasive outpatient surgical technique with no visible incisions in which the patient remains awake and actively participates by providing their opinion throughout the procedure. The technique is indicated for the treatment of more advanced gynoid lipodystrophy where fibrous septa are visible at rest. It involves the sectioning the septa to release the traction they exert on the reticular dermis to result in a smoother and softer skin topography. A needle is inserted to a depth of 6 to 10 mm with movements made parallel to the skin surface to break the fibrous tissue bands. This allows for the redistribution of subcutaneous tension while minimizing adipose tissue displacement [2,3,7,9,16].

**Goldincision®:** Described by Chacur et al. and first published in 2019, Goldincision® is a protocol developed for the treatment of more advanced cellulite. It combines subcision with collagen biostimulation to improve overall skin quality across an entire area and not just at the cellulite itself, and often results in greater

patient satisfaction. The procedure is performed with a holistic assessment, both static and dynamic (with the patient in motion), includes the selection among several products, and is administered in an upright position under local anesthesia [17,18].

**Biostimulators:**

**Calcium Hydroxyapatite:** This is biocompatible, biodegradable, and resorbable biostimulating filler containing calcium hydroxyapatite (CaHA) microspheres that can stimulate endogenous collagen production. A consensus published in 2019 cites recommendations for the use of hydroxyapatite in various areas, including the buttocks and thighs, where it is used to improve skin laxity and the appearance of cellulite. The product is applied primarily to the upper and lateral portions of the buttocks using a fan- or star-shaped cannula [19,20].

**Poly-L-Lactic Acid:** A biocompatible, biodegradable, and bioresorbable polymer. Recognized for its ability to produce collagen and elastin by stimulating regenerative pathways using the body's natural response to foreign bodies. In the buttocks, the product is injected into the upper and lateral quadrants using a linear or fan-shaped retroinjection technique. The anatomical structure of a patient's gluteal region is critical in determining the ideal placement of the product to achieve the desired aesthetic effects [21,22].

**Quality of Life**

Much of the demand for GLD treatments stems from its aesthetic aspect. While not life-threatening, gynoid lipodystrophy significantly impacts patients' quality of life [2].

The World Health Organization appreciates that health is not merely the absence of disease or infirmity and includes an individual's ability to lead a productive and enjoyable life. Employing measurement instruments such as questionnaires and scales to evaluate the influence of certain aesthetic conditions on a patient's quality of life is therefore important to their overall health [2,10]. However, studies on these are relatively uncommon. Validating instruments capable of assessing how much and why aesthetic imperfections impact and disrupt people's daily lives today are of great value [2,10].

Gynoid lipodystrophy is a condition that affects an individual's psychosocial sphere because it is related to their physical appearance and self-esteem and significantly impacts their perception of well-being and social acceptance. Among the impacts of gynoid lipodystrophy on the daily life of sufferers are the choice of more concealing clothes; use of compression garments; avoidance of leisure activities involving body exposure such as at beaches, swimming pools, and massages; restrictions on physical activities such as swimming and water aerobics; feelings of shame regarding body exposure during intimate encounters; and feelings of embarrassment, guilt, frustration, and discouragement [2,10].

**Conclusion**

The impact of gynoid lipodystrophy is more than purely physical. It significantly affects the social behavior and the self-esteem and emotional well-being of patients. Therefore, the significance of an individualized, multidisciplinary approach based on scientific evidence, both in the assessment and treatment of this condition, is evident.

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