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Introduction

lipedema is an alteration or disorder of the distribution of fat tissue, poorly known, which affects exclusively women and involves mainly the lower extremities.

Epidemiological data are scarce and little useful to help us determine the exact incidence of it.

The etiology and pathophysiology of lipedema are not sufficiently clear. The diagnosis is fundamentally clinical, since specific diagnostic tests are lacking or that are supported by sufficient scientific evidence. However, from its clinic aspect it may imply a deterioration in the quality of life of patients, due to the physical, psychological, and social impact that it entails.

Approximately 70% of cases are associated with pain in the extremities, which is why they are usually referred to units of phlebology and lymphology. The treatments directed to the control of the edema do not usually give satisfactory results in the reduction of the volume of the members.

To this are added the conditioning factors of 21st century fashion, where stylized bodies are a claim for most women while the reality is that overweight and obesity increase alarmingly. Approximately 80% of the obese people do not recognize being overweight, which complicates the early diagnosis, the prevention of the evolution of the disease and, consequently, delays the treatment in this group of patients.

Clinical presentation and symptoms lead patients to receive erroneous diagnoses, often mistaken for lymphoedema, obesity, lipodystrophies or chronic venous insufficiency, which is why inappropriate and ineffective treatments are applied and, in the best cases, symptomatic treatments.

Given the lack of unification of criteria and the controversy at national and international level that surrounds lipedema, from the Spanish Association of Lymphoedema and Lipedema (AEL) a multidisciplinary working group was convened, formed by health professionals from different disciplines involved in the diagnosis and treatment of this disorder, to make this Consensus Document.

The goal was to answer many questions with the documented evidence and clinical experience that exists so far.

Is the pathophysiology currently described to explain lipedema sufficient?

Is it a progressive alteration? Does it always evolve towards deterioration?

Is the progressive increase in body fat percentage normal due to lipedema?

If the main symptom is not edema: Is manual lymphatic drainage an essential tool for treatment?

Is it correct to prescribe compression garments in all cases?

What are the most effective treatments?

Participating in this Working Group: The Spanish Association of Lymphoedema and Lipedema (AEL), the Spanish Chapter of Phlebology and Lymphology (CEFyL) of the Spanish Society of Angiology and Vascular Surgery (SEACV), the Spanish Society of Aesthetic Medicine (SEME), the Spanish Society of Reconstructive and Aesthetic Plastic Surgery (SECPRE), the Spanish Society of Dietetics and Food Sciences (SEDCA), the Complutense University of Madrid, and physicians specializing in Physical Medicine and Rehabilitation, members of the Spanish Society of Rehabilitation and Physical Medicine (SERMEF).

This document contains several chapters dedicated to the definition and pathophysiology of lipedema, diagnostic methods, differential diagnosis, classification and its treatment with physical, pharmacological and surgical means. We hope it will help people with lipedema and the professionals who are in contact with them.

However, much remains to be learned about the etiopathogenesis of lipedema, its diagnosis and treatment, so we must continue to investigate and complete the information with epidemiological studies of incidence and prevalence, always from an interdisciplinary approach.

Chapter 1: Definition and Epidemiology

Definition

Lipedema is a clinical entity of a chronic nature, typical of the female sex, with special involvement of the lower limbs, poorly known, underdiagnosed and often confused with lymphedema, lipodystrophies or obesity.

Currently, the World Health Organization (WHO), despite the fact that the European Lymphology Society has recently requested it, does not consider it a disease and therefore does not appear in the International Classification of Diseases (ICD-10- ES), available in electronic version at: http://eciemaps.msssi.gob.es/ecieMaps/browser/index_10_mc.html

In this index of diseases, the term "lipedema" appears on page 264, referring the reader to the term "edema". If we review the term "edema", on page 142 (edema, edematous), it is only considered as "leg edema" (R60.0) with two possible etiologies: "due to venous obstruction" (I87.1) or "hereditary" (Q82.0) which refers to "congenital and hereditary (chronic) lymphoedema (idiopathic)" (Q82.0 on page 263). The term "elephantiasis" appears on page 143. The concept of lipolymphedema does not appear in the classification.

Therefore, at the moment in which this Consensus Document is published, lipedema is not considered a disease by the WHO, although the revision of the ICD 10 (the ICD 11) that is final in the month of May 2018, and which includes among other proposals, the consideration of "lipoedema" and "cellulitis" (PEFE) within the pathology of fatty tissue: <https://icd.who.int/dev11/f/in>

If we follow the definition of WHO disease, such as "Alteration or deviation of the physiological state in one or several parts of the body, for causes generally known, manifested by symptoms and characteristic signs, and whose evolution is more or less "Predictable", lipedema would fit as a disease, as the patient associations consider and claim. However, this Group of experts considers that lipedema, when it is not associated with diseases or aggravating circumstances (obesity, venous or lymphatic insufficiency, osteoarticular alterations, immobility, etc.), may not meet all the criteria to be considered a disease.

Given that currently there are no diagnostic criteria agreed upon and accepted by the scientific community to confirm the presence of lipedema, further studies and lines of research are necessary to establish whether this entity meets the criteria of disease or is an aesthetic alteration that it causes psychological and social distress to those who suffer from it.

It has been considered a rare adipose tissue disease; however, we have observed some confusion in the literature when establishing the differences between lipedema, morbid obesity, lipodystrophies and rare adipose tissue syndromes. In the list of rare diseases and their synonyms published in the Orphanet Newspaper Report - List of rare diseases and their synonyms in alphabetical order in December 2016, lipedema appears with the number 77243.

Allen and Hines described it for the first time in 1940 and called it "Lipedema of the legs". As they published, lipedema is an increase in the volume of members, generalized and symmetrical, usually associated with a progressive increase in body weight, which affects women, in many cases with a family history of similar cases, and which can cause stress and a major concern for the appearance of their legs (Allen and Hines, 1940).

The increase in volume is due to the symmetrical accumulation of adipose tissue, usually in the lower limbs, which affects almost exclusively women, and which barely responds to strategies to lose weight. It is also characterized by pain on palpation and capillary fragility with ecchymosis or bruising at minimal trauma or even spontaneous. Typically, it affects the thighs and legs (respecting the feet) and sometimes the arms.

To all this we must add that edema can present in these patients and can be due to different causes:

- **Orthostatic edema**
Most common type of edema, that worsens through the day and improves with decubitis.
- **Edema associated with venous insufficiency** This group does not consider the term flebolipedema suitable despite existing in analyzed literature, as it contributes to the confusion already present. Chronic venous disorders that can be associated with lipedema, should be denominated according to the classification CEAP according to the a Guía de Práctica Clínica en Enfermedad Venosa Crónica (Abbad, 2015) y el Consenso Interdisciplinario Vein Term (Eklof B, 2009).
- **Edema due to lymphatic insufficiency:** there is controversy about this edema whether it is lymphedema associated with lipedema, constituting the so called lipolymphedema or if it's a secondary lymphedema due to obesity. Given that this is not always present in patients with a high BMI, we consider that they can be present in both situations.

There is an esthetic component that is very important, lipedema can affect physically as well as a psychologically and socially, decreasing their quality of life in a remarkable way.

The term "lipedema" is not really right and gives rise to confusion, given that there is no real edema in all cases, this is more about a fatty pathology

While in Europe it is denominated as "lipoedema", we have preferred to denominate it as lipedema, given that this term is used in Spain in clinical practices.

The terminology confusion is explained by numerous words in the literature to denominate it.

TERMS USED IN LITERATURE TO REFER TO LIPEDEMA

Adipocianosis

Adiposalgia

Segmental adipose

Painful adipose

Edema adipose

Spongy adipose

Dercums disease

Lipalagia

Lipedema

Lipodystrophy

Lipoedema

Liphyperplasia

Lipomatosis painful in the legs

Massive obesity on the lower extremities

Painful column legs

Riding breeches syndrome

Painful fat syndrome

Stovepipe legs

Despite the existing terminology, this Group considers the use of lipedema as the most appropriate to refer to this entity.

Entities such as Dercum's Disease and Lipodystrophies cannot be considered as synonyms for lipedema because they are well-defined diseases and in terms of the terms: "lipohyperplasia" / "painful lipohypertrophy", they are not adequate since they correspond more histological definitions than plaques clinical.

KEY POINTS:

- The lipedema is a chronic clinical entity, typical of the female sex, with involvement of the lower limbs.
- The absence of a clear definition of lipedema leads to great confusion in the literature, both at the epidemiological, diagnostic and therapeutic levels.
- The term lipedema is not very accurate since there is no true edema in all cases, in essence, a disorder of fat
- Despite the existing terminology, this Group considers the term lipedema to be the most appropriate to refer to this entity

- Concepts such as "phlebolipedema" and "lipolinfedema" are debatable despite them being mentioned in the analyzed literature.
- This Expert Group considers that lipedema may not meet all criteria to be considered a disease.

EPIDEMIOLOGY

Epidemiological data are currently insufficient and heterogeneous. Given that the diagnostic criteria are not standardized or consensual, the prevalence data vary from one publication to another, most of which come from clinics or lymphedema units: Among the patients who consult for lower limb edema, Langendoen et al. 2009, they found a 10 to 15% of lipedemas. Földi in 2006 in Germany declared a prevalence in women of 11%, data obtained from an estimate of undiagnosed patients of lipedema in the general population, and who sought medical attention in the clinic. Forner et al. in 2012, the Lyfedema Unit of the La Fe University Hospital in Valencia, Spain, reported that 18.8% of the 843 patients treated in their unit from 2005 to 2011 had lipedema. At present, it is the only prevalence record published in our country. This number oscillated between 8 and 17% of the patients attended in different lymphedema clinics in Germany (Gregl A. 1987 and Herpertz U.1997). Researchers from the Regional Department of Dermatology of the St. Georges Hospital (London, United Kingdom), estimated that less than 0.1% of the women seen in their service had lipedema. However, they emphasize that this percentage is probably underestimated, due to the erroneous diagnosis and the insufficient and inadequate referral of patients by primary care physicians (Child AH et al., 2010). The lipedema affects almost exclusively women. It is presupposed estrogen dependence, taking into account its appearance at puberty and may be aggravated in pregnancy and / or menopause. Only two cases have been described in men, coinciding with hypogonadism and liver cirrhosis (Chen SG, 2004, Langendoen, 2009). Family cases have been described in 15 to 64% (Halk 2017).

KEY POINTS

- The current epidemiological data is insufficient and heterogeneous.
- Due to the absence of clear diagnostic criteria, the real prevalence is unknown.
- It is considered an underdiagnosed and misdiagnosed disorder
- New studies are needed to establish the true prevalence of lipedema in the general population.

CH.2 ETIOPATHOGENIA

Most of the proposed etiopathogenic theories for lipedema try to explain the characteristics of the fatty deposit that affects the lower half of the body, and some of the associated clinical manifestations such as pain and capillary fragility among others.

Numerous etiopathogenic mechanisms have been described, some of them with little scientific basis, which is why they have not been analyzed by this Group; such as mechanisms of intestinal dysbiosis, inadequate clearance of the interstitial space, acidifying diet and use of tight clothing.

LYMPHATIC AND BLOODY MICROCIRCULATORY MECHANISMS

The existence of alterations of the lymphatic circulation associated with lipedema has been proposed, although the alterations of the lymphocytopygraphy described in the bibliography are variable. While Bilancini S (1995) describes a delay in lymphatic emptying, in patients with lipedema in relation to normal subjects, it cannot explain why the findings are asymmetric, although lipedema is always bilateral and symmetric. However, Van Geest AJ (2003), discards them.

Experimental studies such as that of Blum KS (2014) describe a decrease in the frequency of contractions in lymphatics and a reduced response to mechanical stimulation in mice subjected to a fat diet. In this case the alteration of the lymphatics would be secondary to fatty deposits, while authors such as Godoy JMP and Godoy MFG in 2011 and 2012, attribute to the lymphatic stasis a mechanism that favors adipogenesis and relate it to the etiopathogenesis of fibroid edemato paniculopathy sclera (PEFE).

The mechanism of lymphatic stasis is also defended by authors such as Curri SB (1984, 1985, 1986) and Bacci PA (1997) who justify that these lymphatic and blood microcirculatory alterations, due to enzymatic, inflammatory or hypoxia action, can be the cause of excess in the fat deposit (Figure 1).

Amann-Vesti BR (2001) describes the existence of lymphatic microaneurysms in patients with lipedema both at the level of the thigh and the ankle, while they are hardly found on the back of the foot. The author himself recognizes that microaneurysms may be secondary to lipedema and not its cause. Authors such as Fife CE (2010) suggest the existence of microcirculatory blood alterations with formation of neocapillaries in the thickness of fatty tissue that through capillary fragility mechanisms would lead to tissue hypoxia, the formation of bruises and the pain associated with lipedema. However, pain in lipedema has also been attributed to other mechanisms such as nerve compression due to hypertrophy / adipocyte hyperplasia, mechanisms of inflammation or central mechanisms related to chronic pain (Langendoen SI, 2009, Peled W, 2016).

Authors such as Siems W (2005) relate capillary fragility with angiogenesis, which in turn is responsible for tissue hypoxia and find values of Vascular Endothelial Growth Factor (VEGF) 5 times higher in patients with lipedema and / or PEFE than those found in normal subjects.

Szolnoky G (2008) studies capillary fragility by means of a suction method and describes that complex physical therapy allows reducing capillary fragility expressed by the number of petechiae in the treated group versus the control group. We do not know any subsequent works that validate these results, as well as the reproducibility of the method.

Authors such as Földi E (2006) mention a diminished veno-arterial reflex that can contribute to the formation of ecchymoses and bruises associated with lipedema. The clinical perception, makes us think that the mechanisms involved in the greater capillary fragility can also be associated with a functional phenomenon related to menstrual cycles and mediated by hormonal mechanisms. There is evidence of hemodynamic changes that affect the diameter of the veins and the closure of the valves throughout the menstrual cycle (Asbeutah AM, 2014). Alterations of the blood microcirculation were also described by Curri SB in its thermographic classification of "cellulitis" (Curri SB, Merlen JF, 1986). These authors in the 80s already attributed alterations in blood microcirculation with hypoxia and cutaneous hypothermia to the etiopathogenesis of PEFE, but the review on lipedema shows that more recent publications (Fife CE, 2010; Földi E, 2006; Szolnoky G, 2008) have extended these microcirculatory alterations justifying the hypoxia associated with lipedema, as a cause of hypothermia, pain, capillary fragility, fatty deposits and the presence of telangiectasias. Harvey NL (2008) and White MH (2001) also propose the existence of alterations in the structure and function of the lymphatic system. Although this Consensus Group (CG) considers that PEFE can coexist with lipedema, there is not enough scientific evidence to support microcirculatory alterations as etiopathogenic of both entities and these should not be considered the same.

MECHANISMS RELATED TO THE EDEMA GENESIS

In the British Clinical Practice Guidelines for lipedema 2017 (Coppel T, 2017) it is mentioned that lipedema can be accompanied by edema, as was described in the original work of Allen EV (1940) and that this may result from the overload of a normo-functioning lymphatic system. Therefore, edema would not be an etiopathogenic mechanism of lipedema, but this may be associated with orthostatic edema, immobility, systemic or circulatory pathology (venous and / or lymphatic) that could worsen the symptoms (Krijnen RM, 1997, Madeleine P, 1998, Rossi G, 2007, Schmeller W, 2007, Uda S, 1997). It is important to note that by following author like Schmeller W (2007), the participation of mechanisms such as immobility in the genesis of lymphedema since the lymphatic system requires movement and exercise to generate the initial lymphatic transport through changes in tissue pressures. A clinical picture is that of "armchair legs", a term coined by Sneddon I and Church R (1983), refers to patients who spend day and night in armchairs with the lower limbs hanging. Although there is no lymphatic

abnormality, immobility by itself reduces lymphatic drainage and causes functional lymphedema. Over time, the lymphatic vessels can suffer irreversible damage and lead to permanent lymphedema. This mechanism could justify the lymphedemas of morbidly obese patients and justify the worsening of lipedema.

MECHANISMS OF ADIPOGENESIS. LIPOLINFEDEMA

Adipocyte hypertrophy is more related to abdominal obesity (Figure 2) and its metabolic complications, it is more frequent in men and in postmenopausal women; while hyperplasia is usually observed related to genetic factors and occurs in femorogluteal fat (Hirsch J, 1989). In young women the distribution of fat predominates in the hips (gynoid distribution) while with age the fatty tissue of the lower limbs decreases as the central location increases; This change is more evident in postmenopausal women. The distribution of central fat is typical of men (android distribution) and of the elderly woman (Björntorp P, 1996); It is related to co-morbidities (metabolic syndrome, hypertension, insulin resistance and type 2 diabetes) but responds well to diet and fasting, unlike fat located in the lower half of the body.

According to these genetic mechanisms (female sex), hormonal (estrogens) and embryonic development itself, there is a greater deposit of fat in women than men and it is distributed in the lower half of the body as a secondary sexual character. The poor response to diet would respond to the fact that adipocyte hyperplasia is more frequent in the gluteal fat of a young woman.

Suga H (2009) and Schneble N (2016) consider that the increase in subcutaneous fat tissue in lipedema may be due to hypertrophy and / or adipocyte hyperplasia, but they consider it more likely to be hyperplasia because the fatty deposits of the limbs with lipedema do not respond to diet. We have not found histological studies in large population groups that confirm whether there is hypertrophy or adipocyte hyperplasia in lipedema, which is why this group considers it to be just an etiopathogenic theory.

As previously mentioned authors such as Blum KS (2014), Godoy JMP and Godoy MFG (2011, 2012) support the existence of lymphatic microcirculatory mechanisms that stimulate localized adipogenesis in lipedema, while authors such as Hosogai N (2007), Trayhurn P (2008) and Halberg N (2009) attribute the mechanisms of hypertrophy / fat hyperplasia to hypoxia.

The increase of certain markers (Ki67 and CD34) related to the proliferation of adipose and progenitor fat cells has also been described, suggesting a rapid increase in adipogenesis that could in turn cause tissue hypoxia. In this case, hypoxia would be a consequence of excess fat and not the cause.

High plasma levels of malonyl dialdehyde (MDA) and carbonyl protein groups have been demonstrated in patients with lipedema compared to healthy subjects, which decreased after shock wave treatment (Siems W, 2005). These markers of oxidative stress are increased in many other chronic diseases, obesity among them, although it is possible that they lack to know

biochemical mechanisms related to the production of adipokines and increase of inflammatory phenomena that favor adipogenesis (Arner E, 2010; -Donne I, 2003, Ezquerro S, 2016, Jung UJ, 2014).

However, several authors (Buck DW, 2016, Fuster JJ, 2016, Herbst KL, 2012, Jeffery E. 2016) do not associate lipedema with metabolic diseases such as diabetes or hypertension. This may be justified because co-morbidities are more related to central obesity than to femorogluteal fat.

Adipogenesis is accompanied by angiogenesis and macrophages that play an important role in it. It has been observed that, while in normal adipose tissue they constitute between 5 and 10% of all cells, in obese the number of macrophages reaches up to 40%. The study by Cho CH (2007) in the distal adipose tissue of the epididymis of mice showed that macrophages induce angiogenesis through the secretion of metalloproteases and through the activation of the VEGF-VEGFR2 system.

It is possible that much remains to be known about the mechanisms related to adipogenesis and whether they are related to the etiopathogenesis of lipedema or respond to changes related to obesity (Mc Gillcuddy FC, 2011, Tan BK, 2009).

More recent studies find a correlation between fibrosis in the subcutaneous adipose tissue and the greatest difficulty for weight loss after bariatric surgery (Bel Lassen P, 2017).

We have found experimental studies that relate lymphatic stasis with adipogenesis and adipose tissue fibrosis, as well as inflammatory phenomena (Maruyama K, 2005, Hardford KA, 2011, Rosen ED 2002).

Other authors consider lipedema as a masked form of obesity whose clinical diagnosis is relatively simple but whose physiopathological mechanisms are not completely known (Langendoen SI, 2009; Szél E, 2014).

This relationship of lipedema with overweight and obesity, can be seen in the work of Khalaf M (2013) that studies 20 female patients and subjects them to a diet program, decongestive physical therapy and pressotherapy obtaining a significant reduction in the rate of BMI and the volume of the limbs. It is noteworthy that the treated patients were overweight and obese, so the results of improvement with the diet were expected.

This Group considers the need to open new lines of research aimed at the study of adipose tissue as an endocrine organ that produces cytokines, as well as confirming that the blood and lymphatic circulatory mechanisms described in the literature participate in the etiopathogenesis of lipedema despite the limitations that suppose the functional studies "in vivo" at the level of the microcirculation.

This Consensus Group discards liplymphedema as an evolutive picture of lipedema, although functional lymphatic alterations that justify the edema associated with lipedema or organic

alterations can coexist since the incidence of primary lymphatic alterations of the lower limbs in the general population is unknown.

GENETIC AND HORMONAL FACTORS

Lipedema is a chronic alteration of the adipose tissue that almost exclusively affects the female sex (Coppel T, 2017, Lontok E, 2017) so it could be presumed an etiopathogeny linked to sex.

Although there are few studies available, there is some evidence of a genetic predisposition with familial predisposition in 15-64% of patients (Child AH, 2010, Földi E 2006, Schmeller W, 2007).

The genetic variants involved have not been fully identified, but the research suggests that this would be an autosomal dominant pattern with incomplete penetrance (Herbst KL, 2012).

Since lipedema affects almost exclusively the female sex after puberty, this condition could also be explained by the effect of estrogens both on the embryonic development of fat (caudal outline) and after puberty.

The isolated cases of lipedema described in males (Chen SG, 2004; Langendoen SI, 2009) could be explained as secondary to hormonal disorders, since there has been low levels of testosterone found.

The events of anovulatory, pregnancy and menopause should be considered aggravating and not common factors of lipedema.

Hormonal factors such as hypothyroidism, Cushing or genital adipose syndrome could also be aggravating factors when associated with overweight / obesity, mobility limitations and other manifestations such as mixedema.

KEY FACTORS

- There are multiple etiopathogenic theories of lipedema without any of them having sufficient scientific evidence to date.
- We consider that factors such as obesity, immobility, lymphatic and venous insufficiency are aggravating and non-etopathogenic factors of lipedema.
- There are points in common between PEFE and lipedema, although it cannot be said that it is the same entity, but they can coexist.
- It is known that lipedema worsens with overweight and obesity, but they are different entities.
- The term lipolymphedema is used in the literature to define the association between lipedema and lymphedema. However, it is not clear that this association constitutes a clinical entity or an evolutive picture of lipedema, nor that lymphedema is primary or secondary.

CH.3 CLINICAL DIAGNOSIS. DIFFERENTIAL DIAGNOSIS.

CLASSIFICATION

CLINICAL DIAGNOSIS

We agree with Herbst KL (2012) and Coppel T (2017) in that the diagnosis of lipedema is essentially clinical, based on the anamnesis and physical examination since there are no specific complementary tests.

The main findings of the anamnesis and physical examination are:

There is often a genetic predisposition since it can affect several women of the same family.

It affects almost exclusively the female sex from puberty.

It affects the lower limbs bilaterally and symmetrically.

There is a disproportion between the distribution of fat from the lower and upper half of the body, which responds poorly to diet and exercise (Figure 3)



Figure 3



Figure 4

The main sign of lipedema is the increase in fatty deposits at the level of the lower limbs without affecting the foot (Chen SG, 2004, Child AH, 2010), disappearing the normal concavities existing on both sides of the Achilles tendon (Todd M, 2016) (Figure 4); and adopting a typical morphology of legs like an Egyptian column, stove pipe or baggy pants.

Characteristic of lipedema is the distribution of fat over the malleoli, respecting the foot (sign of the ring or adipose groove) (Figure 5). It may coexist with an increase in fatty deposits at the level of the buttocks or trochanteric region ("sign of saddlebags" or "in riding pants"), as well as with PEFE and / or flaccidity. The Stemmer sign is negative. (Figure 6).

5a



5b



Figura 5.
Signo
de sur
adip
respe
y el f.

Figura 6.
le Stemmer
en paciente
con lipedema



The Group raises the question of whether there is lipedema in the upper extremities or whether this location corresponds more to entities such as lipodystrophies or morbid obesity. We have not found evidence of clinical cases in the literature that allow us to state that there is lipedema of upper limbs or its prevalence in the general population. (Figure 7)



Figura 7a y 7b.
Afectación de miembros superiores
en paciente con lipodistrofia.

Pain and / or hypersensitivity to light contact and palpation are characteristic. The cause of pain is multifactorial.

Lipedema is usually accompanied by heaviness of the lower limbs and this symptom usually increases similarly to Chronic Venous Insufficiency (CVI): in situations of prolonged standing, excessive heat, prolonged travel by plane or bus, etc.

Increased sensitivity to cold is also characteristic. Palpation can detect areas of colder skin (hypothermia) and different texture (usually softer).

The occurrence of ecchymosis with minimal trauma is common. But given that this finding is common in women, this consensus group (CG) has considered the need to quantify them, in order to have a clinical sign that can be evaluated objectively.

They can present telangiectasias in a variable way and more frequently in adulthood. We consider that the coexistence of telangiectasias is not a characteristic condition of lipedema, but rather, a coincidence given that grade C1 (telangiectasias and reticular veins) of the CEAP classification is present in more than 50% of women. (Álvarez-Fernández LJ, 2008) (Figure 8).



fig 8

It may be associated with orthostatic edema, as originally described by Allen EV (1940), although the existence of a fovea is minimal or absent. It can also be associated with lymphedema. (Figure 9).



*Figura 9.
Lipedema en paciente obesa
con signos de estasis linfática
(linfangitis y engrosamiento cutáneo).
"Lipolinfedema".*

Other findings associated with lipedema are: decreased elasticity of the skin and connective tissue, less mobility due to pain and joint dysfunction, as well as alterations in the plantar support and joint hypermobility; all factors that cause alteration of the dynamics of the lower limbs and the muscular pump affecting the venous drainage, overloading the function of the lymphatic system and favoring the edema. This GC considers that all these findings are not typical of lipedema, but can coexist with it.

Smeenge J. in 2013 describes a certain degree of muscle weakness, whose presence makes physical activity even more difficult.

Special mention should be made of the psychological affects and stress associated with lipedema as factors that affect the patient's self-esteem, especially nowadays with the importance given to fashion and stylized bodies. Often, these patients have difficulty finding clothes that they are comfortable with, given the disparity of sizes between the upper half of the body and the lower half. A survey conducted in the United Kingdom in patients with lipedema allows the following data to be extracted that are very significant (Fetzer A, 2016):

95% showed difficulties in finding suitable clothing.

60% had limited their social life.

60% felt desperation.

50% felt their sexual life limited.

40% believed that they could have had a different professional development had it not been for lipedema.

We must add the discouraging fact that no matter how much the patients undergo strict diets and periods of intense exercise, the zones of lipedema do not reduce their volume. The repercussions in the personal and work environment sometimes lead to the acquisition of mental disorders such as depression, anxiety and alteration of the body image.

Lipedema impairs the quality of life related to the health of the patients; although there are currently no validated scales to measure it in this population.

CLINICAL CRITERIA FOR LIPEDEMA

- Female gender
- Appearance from puberty.
- Family background.
- Increase in bilateral and symmetrical volume of the lower limbs that respects the foot (sign of the ring or adipose groove).
- Disproportion between the upper and lower half of the body that does not respond to diet or physical exercise.
- The Stemmer sign is negative, and the fovea is minimal or absent.

- Pain with hypersensitivity to light contact and palpation.
- Psychological involvement is frequent.
- The occurrence of ecchymosis with minimal trauma is common

AGGRAVATING / CONQUERING FACTORS

Lipedema can condition a worse quality of life when it is associated with other pathologies of the extremities although there are no validated questionnaires available to establish the degree of affectation.

It is important to rule out, through clinical examination, the coexistence of concomitant factors that could act as aggravating symptomatology such as:

Chronic Venous Disease Telangiectasias (C1), varicose veins associated with venous reflux (C2) (Figure 10) and edema are common of venous cause (C3) of the CEAP classification that can worsen the symptoms of the lower limbs especially related to standing, heat, etc. The coexistence of Chronic Venous Disease should be treated according to Clinical Practice Guidelines according to clinical stage and hemodynamic study results (Abbad CM, 2015).

Obesity and overweight

Although lipedema can be observed in patients with normal weight, underweight, even in anorexic patients, the existence of overweight / obesity aggravates the symptoms of the extremities, especially if it is associated with immobility. It is essential to perform anthropometric measurements (weight, height, BMI, waist circumference / hip circumference) and bioimpedance techniques for the adequate diagnosis of overweight / obesity.

Sedentary / Immobility Lack of mobility

It is common in patients with lipedema due to the mechanical limitation of the increase in limb volume, pain and joint restriction, especially in the hip and knees, especially in older patients. The association of aggravating factors such as obesity, as well as the psychological affectation leads these patients to limit their social life.

Patients with lipedema who remain in normal weight and usually perform physical activity have fewer symptoms, better functional capacity and fewer complications than those who do not. (Coppel T, 2017)

Other causes of edema of the lower limbs

Systemic edema generally is characterized by fovea and can be guided by questioning and physical examination. In the case of coexisting in patients with lipedema they must be adequately studied to treat them specifically. Acute systemic edema (renal, cardiac, hepatic, due to hypoproteinemia, medication) or acute locoregional edema as caused by deep vein thrombosis, due to the vital risk involved

DIFFERENTIAL DIAGNOSIS

Lipedema must be differentiated mainly from two entities with which it is usually confused, lymphedema and obesity, although it can coexist with both (Fife CE, 2010). Obesity presents some clear differences with lipedema, although we cannot ignore that more than 50% of patients with lipedema may have overweight / obesity associated.

- Obesity affects both men and women.
- The distribution of fat in obesity is symmetric, although unlike lipedema its distribution is general. It should be noted that if the fat is of gynoid distribution (buttocks and legs) it poses more diagnostic difficulties with lipedema.
- BMI is increased (≥ 30 in obesity and ≥ 25 in overweight), while it may be normal in a patient with lipedema.
- Dietary treatment allows weight loss and a progressive and uniform reduction of body fat, especially at the abdominal level; Not so with lipedema, which does not usually decrease with diet.
- Bruising and bruising are not common in obesity.
- There is usually no special pain or sensitivity of the skin.

Lymphoedema can be differentiated from lipedema by the following clinical-epidemiological characteristics (Child AH, 2010, Fife CE, 2010, Langendoen SI, 2009):

- It affects both men and women (lipedema is almost exclusive to women).
- It usually affects the back of the foot. The Stemmer sign is positive.
- It can begin in childhood, especially in the case of early congenital lymphoedema, while lipedema usually begins in adolescence.
- Except for some cases of primary lymphedema, there is usually no family history (however, reference to the mother is very frequent in lipedema).
- It can be uni or bilateral, but it is usually asymmetric (the lipedema is bilateral and symmetrical).
- Postural measurements with elevation of the limb can reduce lymphatic edema, especially in the initial stages (this is not the case with lipedema). In the lipedema the decubitus eliminates the orthostatic edema, but there is little variation of the volume of the limbs with decubitus.
- Concomitant bruising is rare.
- Pain in lymphoedema presents different characteristics without so much hypersensitivity to contact.
- The skin is usually thickened in lymphedema (especially in advanced stages), while lipedema, the skin is thin and smooth.

- The review of the published literature is also confusing when lipedema is considered to be compatible with adiposities located at the bitrochateric level, gluteal area and internal face of knees or when reference is made to skin alterations such as "orange peel". (Figure 11). These are entities other than lipedema, although they can coexist.



This Group considers it necessary to establish clear differences between lipedema, lymphedema, PEFE and overweight / obesity gynoid. (Table 1).

Add table pg 26

Other differential diagnoses should be established with:

Rare diseases of adipose tissue and / or lipodystrophies: There are some rare diseases of adipose tissue that are accompanied by fatty deposits and increased body volume but that constitute an entity of their own and should not be confused with lipedema:

The disease of Dercum or painful adiposis, characterized by the appearance of localized accumulations of subcutaneous fat with painful cutaneous plaques.

Madelung's disease or multiple symmetric lipomatosis, where there are masses of adipose tissue in the neck, neck, shoulders, trunk and proximal part of the extremities, preferably affecting men with a history of chronic alcoholism.

Ovarian polycystosis, with increased androgenic production and generalized obesity.
Cushing's syndrome

CLASSIFICATION

There is no adequate classification of lipedema and those that are, are insufficient and not universally accepted. They do not have much clinical utility, given that there has been no clear correlation between the different groups and the severity of the lipedema, its symptoms or its

impact on the quality of life of the patients. They also do not provide prognostic value or follow-up of therapeutic results.

In addition, controversy persists about whether it is a progressive pathology or not, or whether the clinical worsening is mainly due to the association of obesity, venous insufficiency and / or lymphatic insufficiency.

Neither is the change or evolution of some types of lipedema described to others, so, for prognostic purposes, we do not have a useful classification.

Some of the classifications available to date are:

- **Classification of Schingale (Schingale FJ, 2003)**

Distinguishes 5 types of lipedema:

- Type I: adipose tissue is increased in buttocks and thighs.
- Type II: the lipedema extends to the knees, mainly to its internal face.
- Type III: the lipedema extends from the hips to the ankles.
- Type IV: lipedema affects arms and legs.
- Type V: lipolyfedema.

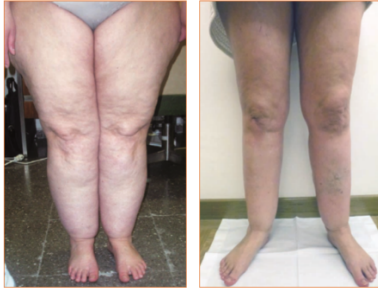
This GC only considers type III of Schingale as lipedema (Figure 12), where the distribution of fat symmetrically affects both lower limbs and especially involves the infrapatellar region, with the characteristic sign of the ring or adipose groove.

As for types I and II, they may correspond to a gynoid distribution of fat as a secondary sexual character and should not be included in the lipedema picture, although they can coexist as with PEFE.

There is not enough scientific evidence to consider lipedema of the upper limbs (type IV) when it is not associated with obesity or lipodystrophies.

The association of lipedema and lymphedema, as previously discussed, can occur in the different phases and stages of lipedema, so it should not be considered as an independent type in the classification.

Lipedema can be observed both in overweight patients (Figure 12a) and in patients with normal weight (Figure 12b).



- **Classification of Meier-Vollrath (Meier-Vollrath, I 2007)**

In line with the classification of Shingale (Schingale FJ, 2003), other authors classify lipedema according to its anatomical location, also defining 5 types, without considering the appearance or not of lymphoedema. (Meier-Vollrath I 2007)

- Type 1: fatty deposits are located in the pelvis, hip and buttocks, without affecting the rest of the lower limb.
- Type 2: the fat is deposited on the thighs, between the buttocks and the knees.
- Type 3: the increase in adipose tissue affects the lower limbs, from the buttocks to the ankle.
- Type 4: lipedema affects the arms and not the lower extremities.
- Type 5: lipedema affects the legs, from knee to ankle, respecting the foot.

Regarding this classification and consistent with the position of this CG, only types 3 and 5 of this classification are considered as lipedema

- **Classification of Schmeller & Meier-Vollrath (Schmeller W, 2004; Meier-Vollrath I, 2004)**

These authors, classify lipedema in three stages according to the changes that occur at the cutaneous level and on palpation:

- Stage 1: the surface of the skin is normal with an increase in soft-tissue subcutaneous cellular tissue in the form of palpable nodules.
- Stage 2: uneven and harder skin surface, due to the presence of accumulations of fat in the form of nodules or lipomas (lipoesclerosis).
- Stage 3: large accumulations of fat that cause lobular deformities on the surface of the skin, especially on the thighs and around the knees. The phenomenon of "orange peel" can be observed when pinching the skin. CIR.

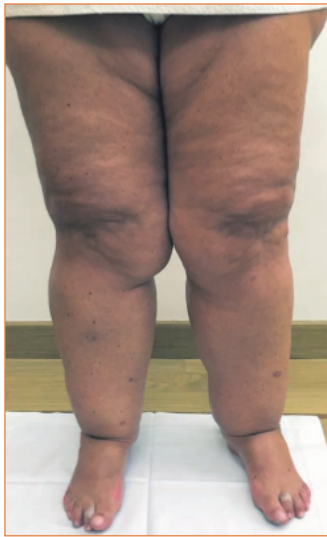
This classification does not discriminate the lipedema of other nosological entities and causes confusion when attributing to the lipedema characteristics characteristic of PEFE such as "orange peel" or palpation of micro or macronodules adipose, so this GC does not consider it adequate.

- **Fonder Classification** (Fonder MA, 2007)

This author makes a classification according to the shape of the members and considers two groups:

- Columnar: lower members in the form of a column or cylindrical. (See Figure 3).
- Lobar: presence of large protuberances or lobes of fat on the enlarged lower extremities, hips or arms. (See Figure 13).

It is just a descriptive classification about the morphology that limbs can present with lipedema, but it does not provide data of clinical or therapeutic utility.



The group of experts that participated in the preparation of the recently published English Clinical Practice Guideline (Coppel T et al., 2017), considers that when classifying patients with lipedema, an approach should be carried out that takes into account its symptoms and functional repercussions, and allow linking to the treatment needs and their response to it. They also suggest that the terms "mild", "moderate" or "severe" are more intuitive than stages and that each degree could in turn lead to the appearance of lymphedema.

As suggested in the recently published Dutch lipedema guideline (Dutch Society for Dermatology and Venerology, 2014), the ICF (International Classification of Functioning, of Disability and Health through which WHO constitutes the conceptual framework for a new understanding of functioning, disability, and health), just as it does to assess other chronic pathologies (Halk AB, 2017).

Based on everything stated, this Consensus Group considered a new classification of lipedema necessary, taking into account the following considerations:

The **adiposities** located on the buttocks and thighs that do not involve the rest of the limb cannot be considered lipedema, although they can coexist.

There is not enough data to affirm that there is lipedema of upper limbs.

The classification based on cutaneous changes does not discriminate the lipedema of other nosological entities such as PEFE.

It is necessary to have classifications that take into account objective clinical data. This Consensus Group proposes to introduce quantifiable clinical criteria to classify patients with lipedema, objectifying, among others, pain and ecchymosis.

KEY PONTS

- The diagnosis of lipedema is essentially clinical based on anamnesis and physical examination.
- There are basic clinical criteria (See table page 25: CLINICAL CRITERIA IN LIPEDEMA)
- Complementary diagnostic methods are usually not necessary except for the differential diagnosis.
- Currently there is no classification of lipedema that includes clinical criteria that can be quantified and allow an objective analysis of the therapeutic results.

CH. 4 SUPPLEMENTARY TESTS

The diagnosis of lipedema is essentially clinical. Complementary methods are usually not necessary except in the case of suspected lymphoedema, in which case the diagnosis of choice would be lymphoscintigraphy (Meier-Vollrath I, Schmeller W, 2004), while for Forner-Cordero I (2010), ultrasound can be considered as the complementary diagnostic technique of first choice for the diagnosis of edema of members of non-systemic cause.

We will analyze the different complementary diagnostic tests and their indication in the study of lipedema.

ANALYTICS

There are no specific complementary tests for the diagnosis of lipedema, although laboratory tests are suggested to rule out associated pathologies that may worsen the symptoms, such as obesity or systemic cause edema. (Herbst KL, 2012, Coppel T, 2017, Forner-Lamb I, 2012, Dutch Guides, 2014).

Therefore, the following determinations should be **evaluated in blood and urine tests**: hemogram (to rule out anemia that justifies asthenia or immobility), glycemia, glycosylated hemoglobin, lipid profile, liver function, thyroid function (to rule out hypothyroidism and subclinical hypothyroidism), urea, creatinine and electrolytes, urine study for renal function, determination of plasma proteins including albumin and insulinemia.

STREETEN TEST

In the Guide to lipedema published in 2017 in England by Coppel T. we found a mention of this test. To do this, the existence of heart, renal and venous insufficiency should be previously ruled out.

The patient takes 20 ml of water per kilogram of body weight and remains upright for 4 hours. Urine is collected during this observational period. The volume of the leg is measured before and after the test. Normal healthy subjects excrete more than 60% of the water ingested and the volume of the leg does not increase more than 350 mL / leg.

The pathological results indicate the existence of a greater permeability of the blood capillaries. Based on the result of the Streeten test along with the clinical characteristics, the diagnosis of lipedema can be suspected, although what this test measures is orthostatic edema.

The Streeten test does not provide relevant data for the diagnosis of lipedema.

LYMPHOCINTIGRAPHY / ISOTOPIC LYMPHOGAMAGRAPHY (LGG)

It consists of injecting a macromolecule marked with a radio-tracer by intradermal or subdermal route in the interdigital space of the extremity to be studied. The tracer is tracked with a gamma camera. These particles of colloids will be distributed in the circulation according

to the surface charge and size; the small diameter colloids are absorbed by the blood capillaries, while those of larger size are absorbed in the lymphatic system.

The time that the radio-tracer needs to appear in the different lymphatic regions depends on the physical characteristics of the colloid used. For example, human serum albumin labeled with technetium 99 may appear in pelvic collectors in 10 minutes, however, other agents such as rhenium and colloid labeled with antimony trisulfide (Sb_2S_3) may take 30 minutes to an hour respectively.

The main advantage of the LGG is that it allows the functional study of the lymphatic system and the diagnosis of lymphedema (Forner-Cordero I, 2010; Sánchez Nevárez MI, 2014) since the qualitative interpretation of the images results in excellent sensitivity (92%) and specificity (100%) for the diagnosis of lymphedema, but it is not useful to distinguish a primary lymphedema from a secondary one (Sánchez Nevárez MI, 2014).

In lipedema, the lymphocytic findings described in the literature are disparate. Bilancini S (1995) describes a delay in lymphatic drainage in patients with lipedema in relation to normal subjects. It cannot explain why the findings are asymmetric, although lipedema is always bilateral and symmetric.

Bräutigam P (1998), is convincing when demonstrating that all the patients studied with pure lipedemas (without obesity) showed normal findings in the double chamber lymphocytopygraphy where the epi and subfascial drainage was analyzed and not only the asymmetry in drainage and visualization of lymph nodes as in the work of Bilancini. Also, it is important to recognize that lymphocintigraphy is not enough to detect differences between normal lymphatic functioning and minimal or functional lymphatic alterations. This author also analyzes the female idiopathic cyclic edema attributed to an increase in microvascular permeability with microangiopathy (in the study with electron microscopy) and that tend to test positive for Streeten. This group showed an increase in radiotracer velocity compatible with dynamic lymphatic insufficiency. The author concludes that lymphocintigraphy is not essential, but it is a useful tool when the diagnosis is doubtful.

Often there are several indeterminate forms of edema, in which the individual etiological components cannot be readily distinguished while the morphological changes described by authors such as Herpetz U (1995) are not necessarily indicative of functional abnormalities since no alterations in function were observed in the lymphatic system of patients with pure lipedema.

We can consider as limitations of the technique:

- Although it can distinguish between different mechanisms of lymphatic failure, especially in primary lymphedemas, it can not necessarily identify a cause of lymphatic obstruction (Sanchez Nevárez MI, 2014, Meier-Vollrath I, 2004).

- Different protocols are described and practiced (Williams WH, 2011), which are not always reproducible.
- **The interpretation may vary depending on the molecule used, the infiltration route (intradermal, subcutaneous), which could justify the disparate findings published with this technique in lipedema (Andrade M, 2011).**

For all these reasons, edema forms should be defined clinically, and clear diagnostic criteria established (Piller N, 2017) before indicating complementary studies such as lymphocintigraphy.

Several authors agree in establishing the value of lymphocintigraphy in the diagnosis of lymphedema, but with variable results in lipedema and other edema.

The lack of systematization in the protocols, as well as the ignorance of the incidence of asymptomatic primary lymphatic alterations in the general population are important limitations for the indication systematic evaluation of LGG in the diagnosis of lipedema; In addition, the LGG findings may not be interpreted in the same way by different professionals (Figure 14).

Although Forner-Cordero I, (2016) refers to lymphocintigraphic alterations in up to 40% of patients with lipedema, it is more frequently used in advanced stages.

Prospective studies should be proposed in this field to unify the LGG protocols (colloids and radio-tracer used, infiltration technique, dynamic studies, interpretation of results, etc.), assess the findings in pure lipedema (not associated with obesity). and / or venous insufficiency), in female cyclic edema and in the general population.

This Consensus Group considers that the indication of LGG should be made by the specialist doctor when the existence of lymphatic pathology is suspected or in the selection of candidates for surgical treatment (liposuction) to rule out the coexistence of lymphatic failure.



FIG 14

METHODS OF DIAGNOSIS BY IMAGE

Conventional systems based on X-rays and advanced technologies, such as computed tomography (CT), ultrasound (ultrasound, echo Doppler, Elastography), magnetic resonance imaging (MRI) and bone densitometry (DEXA), are the diagnostic means most used for the study of skin and subcutaneous cellular tissue affectations, especially those related to tumoral and circulatory processes.

The **DEXA technique** (dual energy X ray absorptiometry) based on the use of photons with low kilovoltage, in addition to the study of bone densitometry allows to analyze the amount and distribution of body fat in the study of overweight and obesity.

Computed tomography (CT) or Magnetic Resonance Imaging (MRI) can be useful in the diagnosis of lymphatic alterations related to tumor pathology or by the characteristic images of the superficial "honeycomb" adipose tissue typical of lymphedema.

MRI helps analyze exceptionally the distribution of body fat and the analysis of edema being the technique of choice for the non-invasive study of arteriovenous and lymphatic malformations. It also provides information about the lymph nodes.

ULTRASOUND (US)

Diagnostic imaging techniques based on the application of ultrasound began to develop around the middle of the last century and it is from the present century that improvements in the image have caused a great advance. Ultrasounds (US) applied to diagnosis have not been shown to have negative biological effects on the tissues that are applied, so they constitute a non-invasive technique that can be repeated.

Within studies based on ultrasound we can distinguish:

- **Two-dimensional or B-mode ultrasound:** based on the emission and reflection of ultrasound waves by different tissues, which are transformed into a grayscale image.
- **Color Doppler echo:** to the ultrasound vascular flow analysis is added by applying the Doppler effect that is based on the frequency changes that occur in the US beam when it affects moving structures, such as blood corpuscles inside the vessels; These changes in frequency are proportional to the blood flow velocity at the point studied. It is the diagnostic test of choice for the vascular study since it allows obtaining anatomical and functional information of the arterial and venous system. It does not give information about the lymphatic system.
- **Elastography:** diagnostic technique based on ultrasound that allows obtaining information about the elastic properties of soft tissues. The tissues are subjected to a mechanical vibration and respond to these compression waves with a response that can be visualized as a color scale that establishes the degree of rigidity of the tissue studied. (Ophir J, 1991).

B-mode ultrasound and elastography allow the study of the skin and the hypodermis and are non-invasive techniques useful for the differential diagnosis between lymphedema and lipedema. For this, high definition ultrasound and high frequency probes (18-22 MHz) are necessary. The great variability of apparatuses, as well as the dependent operator character could be limitations in the reproducibility of these techniques.

The color Doppler echo (with linear probes between 7-12 MHz) is currently the gold standard for vascular study and is indicated in the study of edema of the limbs, especially in acute edemas with suspected deep vein thrombosis, also allowing to measure the thickness of the fatty tissue at the level of the leg.

BIDIMENSIONAL OR MODEL B ECOGRAPHY

High resolution sonography with 18-22 MHz probes allows the study of characteristics of the dermis and subcutaneous cellular tissue, which help differentiate lipedema from lymphedema. (Suehiro K, 2013, Naouri M, 2010).

It is important at the time of performing the test, not to exert any pressure with the probe on the patient, since this alters the results in a remarkable way. The limitations are the difficulty for the reproducibility of these ultrasound patterns since it requires high resolution ultrasound and great experience.

The use of ultrasound with linear probes of 7-12 MHz allows to quantify the thickness of fatty tissue at the level of the leg and provide quantitative data in lipedema although with limitations in obese patients (Marschall M and Schwahn-Schreiber L, 2011) and in the reproducibility of the technique (Asensi V, 2006, Bazzocchi A, 2011).

In the case of lipedema, there are two types of ultrasound patterns according to Suehiro K (2013). In the first, an increase in the thickness of the subcutaneous cellular tissue is observed, with hyperechogenicity (predominantly in regions near the ankle), without ultrasonographic alterations or disruptions in the dermohipodermal junction. In the second, the increase in thickness of the subcutaneous tissue and hyperechogenicity is maintained, but there is a fenestrated pattern in the dermohypodermic region, which partially maintains its structure, without reaching resemblance to the cases of advanced lymphedema. This pattern makes it possible to differentiate echogenic lymphedema from obesity, where there are no dermoepidermal disruptions.

The echographic signs of lymphedema described by Naouri M (2010) that help to differentiate it from lipedema are: increased thickness of the dermis, hypoechogenicity of the dermis and loss of definition of the dermohipodermal junction.

However, according to Monnin-Delhom ED (2002) ultrasound in lipedema shows a homogeneous increase in subcutaneous fat without edema or increased fibrosis.

Marschall M and Schwahn-Schreiber L (2011) propose a classification of the severity of lipedema according to ultrasound criteria. It is the only classification based on ultrasound criteria and that provides objective data on the thickness of the adipose panniculus at the infrapatellar level. Proposed 4 degrees of function depending on the thickness of the hypodermis measured with ultrasound at a point located 6-8 cm above the medial malleolus, the thickness of the skin in healthy subjects being 2.1 mm.

This classification provides objective data that added to the anamnesis and clinical history allows to determine the severity of lipedema, and can therefore be used in the follow-up and evaluation of the response to treatments.

- 12-15 mm: mild lipedema
- 15-20 mm: moderate lipedema
- > 20 mm: serious lipedema
- > 30 mm: severe lipedema

Ultrasound can be considered as the non-invasive diagnostic technique of first choice for the clinical diagnosis of edema of non-systemic causes (Forner-Cordero I, 2010).

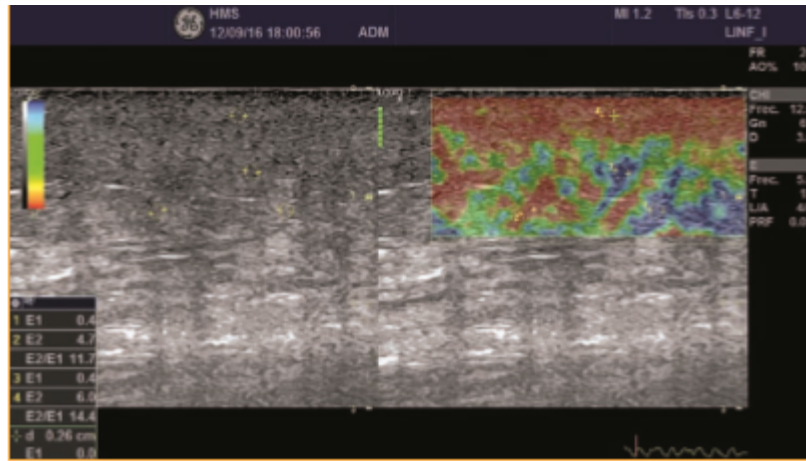
However, **it has limitations:**

- Variability between different devices.
- Long learning curve.
- Variability in the reproducibility of the measurements made, especially at the level of the adipose panniculus (Asensi V, 2006, Bazzocchi A, 2011).
- Limitation for the diagnosis of lipedema in obese subjects (Marschall M and Schwahn-Schreiber L, 2011, Reich-Schupke S, 2013), although this limitation could be excluded by determining anthropometric data.

ELASTOGRAPHY

Elastography is an ultrasound method that allows to visualize the elastic properties of soft tissues and represents an extension of traditional ultrasound.

The purpose of the technique is to quantify or demonstrate qualitatively the elastic characteristics of the examined tissue caused by deformations induced by the hand of the operator (slight compression or vibration). In this way, the combination of B-mode ultrasound and elastography would provide more information on the existence of fibrosis associated with lymphedema, unlike lipedema (Figure 15).



fg15

There are references on the use of elastography in lymphedema (Adriaenssens N, 2012; Onorate A, 2014) although there are no references in lipedema.

This technique would present the same limitations of ultrasound as an operator and dependent device, as well as limitations in the reproducibility of results.

Although there is an increasing number of publications on the utilities of elastography, its use as a first line of study is still limited by its cost, program variation and training needs, although it can provide information in the differential diagnosis between lymphedema and lipedema.

ECO DOPPLER COLOR

The color Doppler echo is currently the diagnostic test of choice for the vascular study since it allows to obtain anatomical and functional information of the arterial and venous system, and of the perivascular tissues, it also allows the study of the thrombus, the differential diagnosis between extrinsic compression (cysts, tumors, etc.) and venous thrombosis, study of edema of the extremities, localization of refluxes at the level of the superficial and deep venous system as well as the study of vascular malformations.

It is performed with linear multi-frequency probe between 7-12 MHz and study program for vascular and soft tissues, this configuration allows both the study of the vascular system and the adipose panniculus of the extremities.

Figure 16a shows the pattern of "lymphatic gaps" (hypoechoic structures without blood flow when applying color Doppler echo) and cutaneous thickening in grade II lymphedema, while Figure 16 b shows homogeneous enlargement of the adipose panniculus in the lipedema

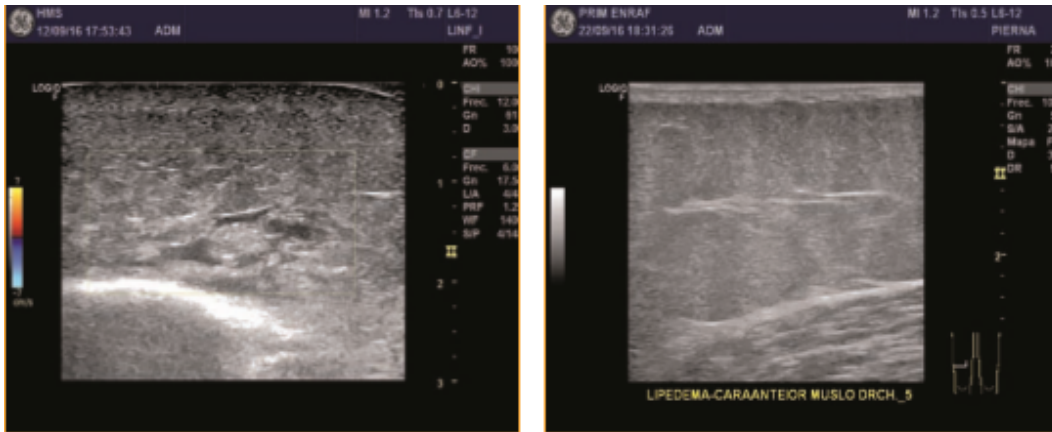


fig16a,b

There is a great variety of devices and programs for arterial and venous vascular study, the learning curve is long, so the echographic examination should be performed by personnel with experience in circulatory pathology.

The color Echo Doppler applied to the study of edema of the limbs allows:

- Discard arterio-venous vascular malformations and arterio-venous fistulas.
- Discard deep vein thrombosis: differentiate between extrinsic venous compression by cysts or tumors and venous thrombosis, study the characteristics of venous thrombi and the post-thrombotic sequelae (obstruction and / or deep reflux).
- Study of the superficial and perforating venous system, analyzing the presence and duration of refluxes spontaneously and after provocation maneuvers.
- Study of the lymph nodes since it has great sensitivity for the detection of ganglion size increase and is useful for preoperative selection and postoperative control in the strategy of lymph node transposition and veno-lymphatic anastomosis. (Sánchez Nevárez MI, 2014).

Along with ultrasound, echo-Doppler is indicated in the study of edema of the limbs as a first line of diagnosis when deep vein thrombosis is suspected or as a complement in the differential diagnosis of chronic edema of limbs when venous disease associated with lipedema is suspected, although this Consensus Group suggests carrying out this procedure routinely to rule out venous refluxes due to the high prevalence of venous pathology in the general population.

COMPUTED TOMOGRAPHY (TC)

The evolution of multi-slice CT allows obtaining a morphological pattern of both the body surface and the deepest planes, with the possibility of quantification and qualification of different territories from the skin, adipose tissue to the musculoskeletal system.

- It is an objective, reproducible and independent operator study to quantify changes at the superficial and visceral fat tissue level.

It presents as advantages:

- It allows an objective, reproducible and independent operator study to quantify changes at the level of superficial and visceral fat tissue.
- Allows the diagnosis of extension of arteriovenous malformations to know if they affect only the skin or reach deep levels, which makes it possible to plan treatments.

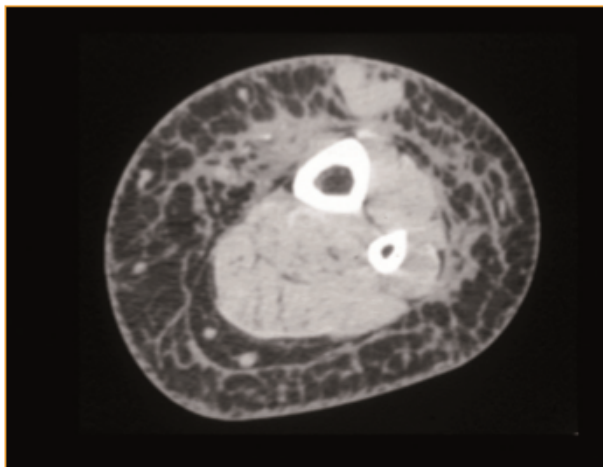
However, its limitations are:

- High cost
- Irradiates the patient, which limits its use as a technique applied to the diagnosis of lipedema and in monitoring the therapeutic response.

According to Monnin-Delhom ED (2002), computed tomography has a sensitivity of 95% and a specificity of 100% for the diagnosis of lipedema where an increase of the adipose panniculus with little or no edema is observed.

The thickening of the skin may appear in lipedema, but the accumulation of subcutaneous fluid, the pattern in "honeycomb" and the involvement of the muscular compartment are typical of lymphedema and are not seen in lipedema.

The changes associated with lymphedema are characteristic and are located at the level of the skin (cutaneous thickening) and subcutaneous plane outside the superficial fascia (increased thickness with typical images in "honeycomb" -Figure 17-) with variable muscle commitment, this makes it possible to differentiate lymphedema from other types of edema such as edema associated with venous thrombosis. In venous edema, the extra and intrafascial compartments are affected.



The role of CT in the study of patients with edema of the lower limbs is to exclude any abdominal-pelvic obstructive mass that can generate lymphedema (Sánchez Nevárez M, 2014).

MAGNETIC RESONANCE (MRI)

Magnetic resonance imaging (MRI) or nuclear magnetic resonance imaging (NMRI) is a non-invasive imaging technique because it does not use ionizing radiation.

Its advantages are:

- It allows to evaluate the fatty tissue in a non-invasive way applying a specific sequence for the analysis of the images.
- It is specific to differentiate fat edema through the application of images weighted in T1, T2 and fat saturation (fat sat).
- Does not irradiate the patient.

Its limitations are:

- Its high cost.
- The impossibility of studying patients with ferromagnetic implants and pacemakers.
- That to study superficial adipose tissue and obtain images of good quality, it is necessary to use 1.5 tesla or 3 tesla MRI equipment with surface coils that allow to obtain more detail of the superficial structures which limits its availability for follow-up of the results of the treatments.

In the work of Monnin-Delhom ED (2002) no significant differences are found in the intensity of the signal between the normal limbs and with lipedema when studying sequences in T1 and T2 and post Gadolinium in T1. In lipedema an increased thickness of the adipose panniculus is verified without evidence of edema.

The findings in lipedema are:

- The skin is not thickened
- There is an increase in thickness of the homogeneous and symmetrical subcutaneous tissue without fluid infiltration or muscle involvement (Figure 18).

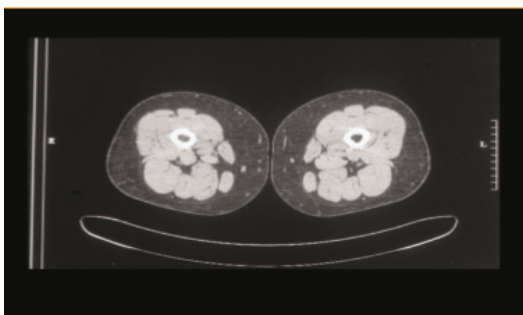


fig 18

As in CT, in the Magnetic Resonance, the "honeycomb" image of lymphedema is characteristic. These images are due to edema because they can be modified with drainage techniques,

coincide with anechoic findings on ultrasound and all these characteristics are typical of fluids. (Figure 19)

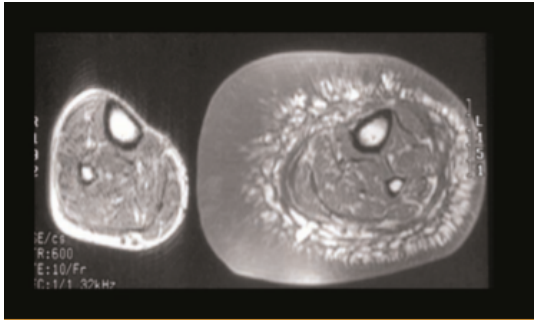


fig 19

MRI also allows the diagnosis of other edema of the limbs, such as the involvement of the muscular compartment that is only observed in edema due to venous thrombosis (Figure 20).

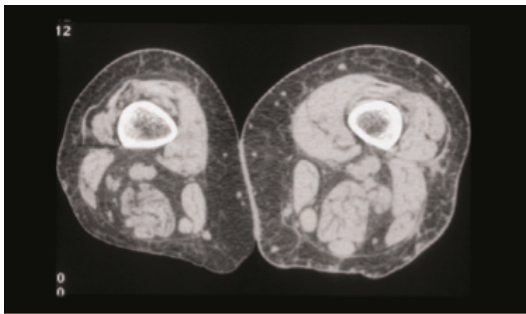


fig 20

A special application of MRI is Magnetic Resonance Lymphangiography (LRM) or Magnetic Resonance Lymphangiography (MRL) that allows a non-invasive study of superficial lymphatic circulation in case of diagnostic doubts.

The main application of MRI in the study of edema of the lower limbs is the diagnosis of lymphedema and would not be indicated in lipedema, except in case of diagnostic doubt, although as we have seen, it is a non-invasive technique that allows differentiation between fatty tissue from edema.

OTHER COMPLEMENTARY DIAGNOSTIC TECHNIQUES

LYMPHATIC MICROCIRCULATION STUDY TECHNIQUES

Direct lymphatic surgery such as lymphovenous anastomosis and lymph node transfer in the treatment of lymphedema have led to the use of minimally invasive lymphatic microcirculation techniques capable of providing information on superficial lymphatic circulation, as well as detect abnormalities such as dermal reflux (Lee BB, 2013). Among these techniques is **indocyanine green lymphography for the follow-up of surgical interventions on the lymphatic system due to its non-invasive character and the absence of radiation as in conventional lymphoscintigraphy** (Yamamoto T, 2011, Chang DW, 2013).

CONTACT THERMOGRAPHY

Contact thermography with microencapsulated liquid cholesterol crystals allows to quickly and easily detect changes in body temperature at the level of the region under examination. These changes are mainly based on the circulatory changes of the region, so there are variations depending on the subject and the environmental conditions at the time of the determination. There are also heat-sensitive infrared cameras capable of graphically recording these findings. The procedure is susceptible to the environment and subjective variations of the observer, which limits the reproducibility of this method (Figure 21).

The most important problem is the environmental temperature variation, so to minimize these variations, it is suggested that before the examination the patient is at rest, preferably in the supine position, at least 20 minutes in a room between 22 and 24° C. The obtained images can be evaluated according to the thermographic classification of the PEFE of Curri SB (1985) in four grades:

Stage 0: Uniform image. Normal.

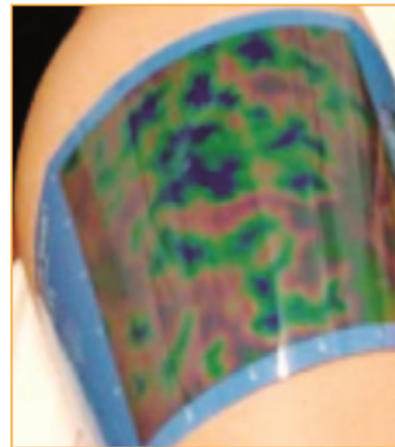
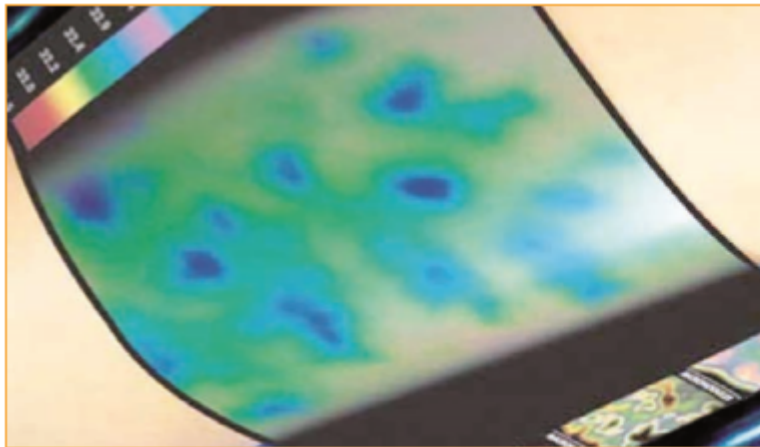
Stage I: Image with spots. Edema.

Stage II: Altered microcirculation.

Stage III: Areas with micronodules ("leopard skin").

Stage IV: Areas with macronodules ("black holes").

Although there is no description of typical thermographic findings in lipedema, their findings would correspond to the degree of hypothermia described in the clinical signs.



DENSITOMETRY FOR ABSORPTION OF X-RAYS (Dual Energy X-ray Absorptiometry) DEXA

Widely used for the calculation of bone mass (densitometry), allows studies on the entire body and know the regional distribution (visceral and peripheral) of fatty tissue. It presents good correlation with anthropometric data. In the study of obesity is used primarily to assess the total fat mass of the patient before and after treatment. The main advantages of the method include its low dose of radiation, the study time for body composition, which is approximately 12 to 15 minutes, and the good resolution of the image at the total body level, although there are limitations: its cost and, although at low doses, it uses ionizing radiation.

There are authors who consider that **the use of this technique is very useful both in the monitoring and in the therapeutic control of lipedema and lymphedema since it allows the study of the volume changes of the limbs and their relationship with the variations of the fat and water** (Brorson H, 1998, 2009).

DETERMINATION OF BODY COMPOSITION THROUGH BIOIMPEDANCE

To establish a correct diagnosis of overweight / obesity, it is necessary to complement the anthropometric data with the determination of body fat percentage through Bioimpedance.

This technique has advantages: simplicity, non-invasive character, reproducibility, absence of interoperator variability and easy application in clinical practice. It allows obtaining reliable and reproducible values of body composition (Pérez Miguelsanz MJ, 2010).

The bioimpedance devices use the electrical properties of the organism to measure the passage of a very low voltage electrical current through it. The technique consists of administering an electric current between two separate points of the organism and measuring the resistance to the passage of that current. Resistance is very low in fluids (blood, urine) which means they are good conductors of electricity. The resistance is maximum in bones and fat so, when body fat increases, resistance increases.

It is important to keep in mind that the devices do not directly measure body composition, they only estimate it from the measurement of the current and its modifications when passing through the body. The analysis of these variations compared with reference patterns in the software of the device allows to calculate total body water, fat-free mass or lean mass and fat mass in relation to height, weight, age, sex and race or ethnic origin of the individual.

Bioimpedance techniques applied to the study of body composition allow a more accurate diagnosis of overweight / obesity, as well as monitoring the response to treatment.

STUDY VOLUMETRY STUDY TECHNIQUES

These techniques have a clear indication in the follow-up of lymphedema and its quantification and should be applied to the follow-up of the therapeutic response in lipedema, however not all of them are of habitual use, so this Consensus Group highlights the usefulness of the circumetry / perimetry for monitoring the therapeutic results in lipedema, as well as knowledge

of the different techniques currently available for the study of limb lymphedema, among which are:

- Volumetric displacement of water from the limb : it is considered the reference method, but it is rarely used in clinical practice, given the "discomfort" of its performance (Figure 22).
- Infrared Perimetry, uses infrared light to measure the contour of the limb and calculate the volume. Its high cost limits its use in clinical practice.
- Circometry / perimetry: it is the most used method in clinical practice, because it is simple, innocuous and valid. (Figure 23)



CIRCOMETRY / PERIMETRY

It involves manual measurement with a simple tape measure, of the perimeters of the extremities at regular intervals of 2 to 4 cm or taking anatomical references.

There is no single validated way to perform the measurements, but the most widespread is the one described by Mortimer PS (1990) from the ulnar styloid, every 4 centimeters, proximally to the upper extremity. In the lower limb we can take as reference the external malleolus and make measurements every 4/6 cm. This measure has to be taken into account since, when calculating the volume according to the formula of the truncated cone, it will be the "h" of the formula.

For the indirect measurement of the volume (V) of the extremities, applying the formula of the truncated cone: the measurements will be: "h" segment measured and "c" the different circumferences of the cone. The limb is considered as the sum of different segments that are assimilated to truncated cone figures.

$$V = (h (c_1^2 + c_2^2 + c_n^2)) / \pi$$

Fórmula del cono truncado

It is important that the reference points for taking measurements are always the same, to be able to follow the patients and see the evolution of the volume of the members.

In unilateral lymphedema the two extremities should be measured, and the indicative value of lymphedema is usually established with a difference of more than 2 cm between both limbs or according to the volume difference expressed in milliliters or as a percentage, compared to the healthy contralateral limb.

Likewise, lymphedema is considered if the excess volume of the affected member exceeds 10% with respect to the contralateral one.

Depending on the severity of the lymphedema (percentage of excess volume of the limb with lymphedema with respect to the healthy contralateral), 3 grades are defined according to the International Society of Lymphology (2003):

- Mild: <20% excess volume of the limb
- Moderate: 20-40% of excess limb volume
- Severe: > 40% of excess limb volume

In bilateral lymphedema, these measurement techniques allow to assess the volume changes of the limbs after treatments.

These techniques are validated for the diagnosis and monitoring of the therapeutic response in lymphedema, but their indications are not standardized in the diagnosis / follow-up of lipedema.



fig 23

ADD CHART PG 46 AUMENTO BILATERAL

KEY POINTS

- The diagnosis of lipedema is essentially clinical, and no complementary tests are usually necessary except in the case of suspected lymphedema, where the diagnostic method of choice is lymphoscintigraphy.
- Diagnostic imaging methods are not essential, but they may be useful in monitoring variations in adipose tissue thickness and volume of limbs in response to treatments.
- The main limitation of complementary techniques such as lymphoscintigraphy, ultrasound and circumetry is its reproducibility.
- The limitation of MRI is its high cost, although it would be the technique of choice in the diagnosis, since it is a non-invasive technique able to discriminate between fatty tissue and limb edema through studies weighted in T1, T2 and "fat sat". "
- Differential diagnosis of lipedema should be made with overweight / obesity through anthropometry, bioimpedance and, if possible, incorporate imaging techniques such as DEXA.
- The cost, effectiveness and reproducibility of complementary diagnostic methods in lipedema is important in order to analyze the results of the different therapeutic procedures with scientific evidence.
- Ultrasound and EcoDoppler are complementary diagnostic techniques of first choice to complement the clinical diagnosis of edema of non-systemic members.
- High resolution ultrasonography makes it possible to differentiate lymphedema from lymphedema and establish the severity of lipedema depending on the thickness of the adipose panniculus, being a useful tool in the diagnostic approach and follow-up.

CH.5 CONSERVATIVE TREATMENT

PHARMACOLOGICAL TREATMENT

Except for the treatment directed to pain, whose ethiopathogenesis is multifactorial and which will be the subject of a section in this chapter, in none of the reviewed works have we found evidence that pharmacological treatment has clinical benefits in lipedema.

Although no studies have been published to support the use of phlebotonics or lymphodrugs in lipedema, its use would be appropriate in those cases with associated edema in order to reduce it, improve its evolution and control its complications. They could also contribute to the improvement of the heaviness associated with heat and the treatment of the symptoms of chronic venous disease (Abbad CM, 2015), given their actions (increased venous tone, decreased capillary permeability and increased lymphatic flow) .

The use of diuretics would not be indicated since there is no true edema, but an increase in the thickness of the adipose panniculus. The coexistence of edema may be due to a systemic cause, or to immobility, associated venous or lymphatic insufficiency. In each case the therapy must be personalized and according to the diagnosis.

TREATMENT OF PAIN

Pain is usually triggered by small stimuli such as pressure on the skin or simple palpation of the subcutaneous adipose tissue. Patients usually refer to it as having mixed, nociceptive and neuropathic characteristics, in many cases accompanied by phenomena that suggest peripheral and / or central sensitization, manifested as hyperalgesia, or allodynia. Lontok E (2017) relates it to the compression of nerve endings, and associated with inflammatory phenomena.

Increased joint pain has been reported, especially in knees and hips, related to poor joint alignment and hypermobility derived from hypermobility. We must also take into account degenerative changes motivated by greater weight overload (Hodson S, 2013).

Usually common analgesics are indicated, although patients with clear neuropathic pain, or signs and symptoms that lead to an alteration of sensitivity should be treated with specific drugs, such as gabapentin.

It is convenient an adequate assessment of pain through validated scales. The questionnaire "Douleur Neuropathique-4" (DN4), validated in Spanish (Pérez R, 2007), consists of 10 items, with descriptions and signs of pain; it is easy to score (each positive item scores 1) and a total score of 4 or more (out of a maximum of 10) suggests the existence of neuropathic pain. (SEE ANNEX 3).

As will be seen in the corresponding section, liposuction has also been shown to be effective in reducing pain (Schmeller W, 2006, Warren AG, 2007).

In the field of aesthetic medicine, the use of mesotherapy / intradermotherapy with authorized draining drugs also causes temporary improvement of the symptoms of pain and heaviness of the limbs in patients carrying lipedema, however, further studies are needed to validate this technique.

KEY POINTS

- Since the origin of the pain that appears in patients with lipedema has not been clarified, there is no specific protocol to treat it.
- Proper characterization of pain is suggested through the use of a validated scale.
- Compression therapy, manual lymphatic drainage, liposuction and specific pain drugs with neuropathic characteristics have been shown to be useful in reducing the pain characteristic of lipedema.
- More studies are needed to validate with scientific evidence the indications of each of these techniques in pain therapy associated with lipedema.

COMPRESSIVE THERAPY

Compression therapy has been shown to be useful in reducing pain when appropriate garments are worn and used correctly by patients (Williams A, 2016). The compressive therapy used in combination with manual lymphatic drainage (MLD), is especially effective in pain control (Todd M, 2016). Compression is an active force exerted by an external mechanical means endowed with elasticity. Containment is passive and mechanically opposed to an increase in volume related to muscle contraction. Although normally speaking only of compression, in practice the compression / containment action is inseparable. Compressive therapy includes different modalities:

1. COMPRESSION CLOTHING: A distinction must be made between:
 - Types of garment: Depending on the morphology of the patient, leotard-type socks may be used, or the foot may be left free with leggings or knee-length stockings (Fig. 24 and Fig. 25). In turn, compression garments use different fabrics:
- It is necessary to distinguish between:



Figura 24.
Prenda de compresión
en lipedema:
media corta tejido plano.



Figura 25.
Prenda de compresión
en lipedema:
panty tejido circular.

- **Types of fabric:**

A) Circular fabric. They are cylindrical garments, and cannot adapt to large deformities. It is necessary to take into account the compression exerted at the level of the ankle and that patients with lipedema are characterized by having an increase in the fatty deposit at the malleolar level, with a sudden change in the volumes between the foot and the ankle. For this reason, these garments can produce "cuts" in this region, achieving the opposite effect to the desired one.

B) Flat fabric. The fabric is knitted and sewn with a flat seam that allows adaptation to large deformities. The fabric is thicker and less elastic than that used in circular garments and is less aesthetically visually.

- **Degrees of compression:**

There are different degrees of compression, depending on the country of manufacture of the garments. So far, no unifying criteria have been achieved at European level.

Inserto table pg51

It is important to emphasize that the therapy with compression garments will not lead to a reduction in the thickness of adipose tissue.

The prescription of compression garments in lipedema will be made individually, since we consider its use unnecessary in all cases. We cannot "enclose" in a compressive garment all women with lipedema if they do not have associated edema, the purpose in this case being to contain it and prevent its progression.

It is important to take into account the difficulty in using these garments, since their placement is not easy, and less so in obese people with little flexibility and in a situation of dependency for their personal hygiene. In these cases, the use of adjustable garments with Velcro can be a solution.

The use of compression garments is recommended at least for physical exercise (Hardy D, 2015; Forner-Cordero I, 2016), prolonged travel by plane, in people whose work requires a long time standing and when associated orthostatic, venous and / or lymphatic edema.

The rejection of the use of compression garments represents a handicap for maintaining the results of the therapy. A high percentage of patients leave the therapy due to the apparent absence of clinical improvement or even worsening of the symptoms, due to an incorrect adaptation of the garment to their needs, either due to an inadequate choice of size or the degree of compression.

In many cases a more flexible strategy is desirable, initially using less compression and, once the adherence to the therapy has been achieved, increasing it to the effective level of compression.

Different practical recommendations have been described regarding the use of elastic stockings:

- Make sure that the garment fits well, avoiding folds, especially in knees and ankles.
- Carry out practical demonstrations on the placement of the compression garment, supervising the patient.
- Inform about assistive devices for the placement of the garment.
- Warn the patient about the clinical signs or symptoms for which the compression garment should be removed, as in the case of pain, paresthesias or dysesthesias, or alterations in the color of the limb.
- Awareness of the beneficial role of elastic support in the control of lipedema, such as the improvement of symptoms and mobility, although volume reduction is not achieved.
- Explain the care required by the compression garment following the manufacturer's recommendations.
- Assess the time of revision and re-evaluation of the type of garment, such as replacement, adjustment of the degree of compression or type of garment, among others.

There is no evidence at present that compression therapy can avoid the risk of suffering from associated lymphatic insufficiency (Fonder MA, 2007, Langendoen SI, 2009, Todd M, 2010).

This Consensus Group coincides with authors such as Reich-Schupke S (2017) and Coppel T (2017) that establish that **the indications for compressive therapy in lipedema are:**

- Reduce pain.
- Improve comfort. Patients feel more comfortable when they wear stockings because of the feeling of support.
- Help to slightly reshape the extremities allowing an improvement of mobility.
- Contain possible associated edema.

Compressive therapy has **contraindications** that should be assessed before prescribing a compression garment. It is essential to verify that there is no arterial compromise, acute heart failure, skin ulcerations, peripheral neuropathies or associated neurological disease, and / or severe distortion of the limb shape that prevents the correct adjustment and adaptation of the garment.

Indications of compression grades

Always under medical prescription, and in a personalized way, these can be some of the indications of the garments according to the compression class (mmHg):

- **Class 1 from 15 to 23 mm Hg:** mild venous insufficiency (tired legs), incipient varicosis of the pregnancy, orthostatic edema prevention, lymphedema prevention (stage 0/1).
- **Class 2 from 24 to 33 mm Hg:** moderate venous insufficiency with truncal varices, post-varicose surgery, post-sclerotherapy, prevention of deep vein thrombosis, stage 1/2 lymphedema, post-liposuction.
- **Grade 3 from 34 to 46 mm Hg:** severe venous insufficiency with cutaneous trophic changes, post-thrombotic edema and stage 2/3 lymphoedema in the lower extremities.
- **Grade 4 higher than 49 mm Hg:** venous ulcer, severe lymphoedema in lower extremities.

2. COMPRESSIVE BANDAGE:

It has no indication in lipedema, unless there is an associated lymphatic component, in which case the use of inelastic bandages associated with complex decongestant therapy (TDC) will be necessary. (Figure 26)



fig 26

3. ADJUSTABLE GARMENTS WITH VELCRO

They can be used as therapy in the reducing phase or as a maintenance measure in the treatment of associated lymphoedema.

4. INTERMITTENT PNEUMATIC PRESSOTHERAPY

Through pneumatic compression boots that will be treated later.

KEY POINTS

- Fat tissue is not reduced with compression.
- Compressive therapy is indicated in case of orthostatic edema, venous insufficiency or lymphoedema associated with lipedema.
- It is also used for its effects in improving pain, supporting tissues and helping to reshape the extremities.

DIETETICS AND NUTRITION

Estimates from the World Health Organization (2017) refer to an increase in overweight and obesity worldwide: in 2016, 39% of adults aged 18 and over (39% of men and 40% of women) were overweight.

In Spain, the prevalence of obesity in adults is 18% in women and 13% in men. In people older than 65, it affects 31% of men and 40% of women.

Obesity in Spanish children and young people is among the highest in Europe (16% of boys and 12% of girls).

Morbid obesity in Spain has gone from 1.8 out of every 1,000 inhabitants to 6.1 out of every 1,000 inhabitants in 2006 (Spanish Society of Cardiology). This represents 1% of the population (in the USA they have morbid obesity between 5% -6% of the population). Women suffer the most from morbid obesity (6.8 out of every 1,000 women and 5.4 out of every 1,000 men).

In the etiology of obesity, genetic and environmental factors have been described, but the action will be directed mainly to the control of these, since the severe hypocaloric diet prevents or reverts obesity even in people with a high genetic load. The number of adipocytes is fixed in childhood and adolescence and is higher in obese than in thin subjects. Around 10% of adipocytes are renewed every year.

We define overweight / obesity as the increase of the body's energy reserves in the form of fat with increased adipose tissue.

According to the BMI, we consider: overweight: BMI ≥ 25 Kg / m² and obesity: BMI ≥ 30 Kg / m²

Diagnosis will be carried out through: interrogatory, physical examination, anthropometry (size determination, weight, Body Mass Index (BMI), waist / hip measurements), bioimpedance techniques, imaging techniques (mainly ultrasound and DEXA), and analytics.

It is important to establish the distribution of body fat according to the waist/hip index (C/C):

- Android or central adiposity: (visceral and extraviseral) is associated with comorbidities (hypertension, type II diabetes, cardiovascular and oncological risk).

Quotient C / C > 1.0 (male) and > 0.9 (female)

- Gynoid or peripheral adiposity: may be associated with circulatory alterations (venous, lymphatic), skin alterations (friction zones) and the dynamics of the March.

Quotient C / C < 1.0 (male) and < 0.9 (female)

Therefore, the diagnosis of overweight / obesity and its treatment occupies an important place in patients with lipedema. Both factors aggravate the clinical picture and can lead to psychosocial problems, so they should be treated.

Patients with lipedema who remain at normal weight and usually perform physical activity have fewer symptoms, better functional capacity and fewer complications than those who do not (Coppel T, 2017).

For the maintenance of body weight, it is essential to balance the intake and energy expenditure (represented by the basal metabolism, thermogenesis and physical activity).

It is important to consider that energy expenditure varies with age, sex, and / or percentage of body fat, factors that should be taken into account when deciding treatments and especially in maintenance of the disease. Physical activity, which includes programmed physical exercise and daily activities (walking, climbing stairs, shopping, maintaining posture, etc.), is very variable from one individual to another.

The objectives of the treatment of overweight / obesity are:

- **Medical:** avoid comorbidities and their deleterious effects on health.
- **Social:** improve the quality of life and self-esteem.

The treatment of overweight / obesity is well systematized and includes:

- **Diet:** The energy intake must be decreased in a variable way depending on the individual (age, sex, percentage of fat mass) until a negative energy balance is reached in order for the body to obtain the energy necessary for its operation, from fatty deposits. This is obtained with a hypocaloric diet, or special diets and adapted in a personalized way as the diets of protein contribution or Very Low Calory Diet (VLCD).

Obesity is a chronic process, so the diet will be planned to be maintained in the long term.

Although the diet mainly reduces the fatty deposits at the abdominal level, there is an effect of reduction of the total body volume and of the fat mass even in the limbs with lipedema, although this decrease in volume is lower in the lower half of the body. that for the normalization of the volume of the lower limbs, complementary treatments may be necessary once normal weight has been achieved and maintained.

- **Physical exercise:** The benefits of physical exercise in general will be analyzed in detail; complementing the practice of physical exercise programmed with the increase of physical activity linked to daily activities.

- **Pharmacological treatment:** Pharmacological treatment is indicated along with moderate hypocaloric diet, in patients with obesity (BMI ≥ 30) or overweight (BMI ≥ 27 to 30) who have at least one comorbidity associated with weight. Orlistat is a specific inhibitor of gastrointestinal lipases that prevent the hydrolysis of dietary fat and is administered orally. Liraglutide is an analogue of the glucagon-like peptide-GLP-1- that binds to and activates the receptor, potentiating glucose-dependent insulin secretion in pancreatic β cells, injectable route with indication in type II diabetes, and treatment of obesity. Naltrexone 16 mg / Bupropion 360 mg (Mysimba®), naltrexone is an antagonist of opioid receptor and bupropion, a weak inhibitor of neuronal reuptake of dopamine and norepinephrine with central action. Approved by FDA, but not currently available in Spain: Phentermine 7.5 mg / Topiramate 46 mg (oral); Lorcaserin 10 mg

- **Surgical Techniques:** For the treatment of morbid obesity, psychological stability of the patient and long-term commitment is essential. It includes techniques such as bariatric surgery (gastric bypass), restrictive techniques (adjustable gastric band, tubular gastrectomy) or endoscopic techniques such as intra-gastric balloon.

KEY POINTS

- Overweight and obesity are frequently associated with lipedema and are an aggravating factor that worsens mobility, favors osteoarticular complications and affects the quality of life and self-esteem of patients.

- It is essential to rule out overweight / obesity in patients with lipedema through anamnesis, physical examination, anthropometric techniques (size determination, weight, body mass index (BMI), waist / hip measurements) and blood analysis (to rule out comorbidities).

- Overweight / obesity treatment should always be performed in patients with lipedema to reduce the complications associated with it.

- It is suggested to perform bioimpedance techniques as they provide data on the percentage of water and body fat and their changes after treatments.

- Imaging techniques (DEXA, ultrasound, etc.) provide complementary information on the location of fat (visceral and superficial) and allow monitoring and objectification of therapeutic results.

- Patients with lipedema who remain at normal weight and usually perform physical activity have fewer symptoms, better functional capacity and fewer complications than those who do not.

REHABILITATION TREATMENT: PHYSIOTHERAPY AND PHYSICAL EXERCISE

The therapeutic objectives of conservative treatment should be focused on reducing pain, improving mobility, managing obesity, preventing secondary joint problems, minimizing the impact on the ability to carry out activities of daily living, improve the appearance of the extremities and encourage self-care (Coppel T, 2017).

The terms used internationally to refer to the conservative therapy that we apply in lipedema are: "Complex physical therapy" (TFC), "Complex decongestive therapy" (TDC, this is the most used) or "Complex decongestant physiotherapy". When applied to patients with lymphedema, it is also called "Lymphedema Decongestive Therapy" (TDL).

The TDC consists of a set of therapies indicated for the treatment of edema. It includes manual lymphatic drainage (DLM), compression and containment therapy through garments, intermittent pneumatic pressure or bandages, postural care and specific exercises, as well as skin care to avoid infections in particular.

It has been considered for many years that TDC is the treatment of choice for lipedema. However, when the therapy is applied in order to decrease the volume of the legs in patients who do not have any associated component of edema, this usually fails, and is even ineffective in some patients with edema, caused by a combination of mechanical insufficiency. and dynamic, without affecting the lymphatic system (Langendoen SI, 2009, Dutch Guides, 2014).

It is necessary to inform patients with obesity associated with lipedema that, to obtain good results in the treatment, it is recommended to lose weight and increase physical activity and simultaneously to start with Decongestive Therapy.

If there were alterations of the walking and of the plantar support, they should also be corrected in order to improve the dynamics of walking.

The DLM is a very specific type of massage, which must be performed by specialized physiotherapists and is designed to improve physiological drainage, stimulating the activity of the lymphatic vessels and eliminating excess liquid and macromolecules from the tissues (Torres M, 2006) .

Other effects that we can attribute to DLM are the reduction of inflammation and the relief of symptoms such as pain. Its analgesic effect would be justified by the gentleness in the pressure of the drainage maneuvers (usually below 70 mmHg), the repetition of the movements and the low speed produced by the stimulation of the mechano-receptors of the skin generated by "Control Gate "the activation of pain inhibitory neurons.

In addition, it has an effect of regulation of the Autonomic Nervous System, generating a decrease in the activity of the Sympathetic Nervous System and consequently increasing the Parasympathetic. Through this effect, we achieve a feeling of well-being in the patient because

it relaxes, reduces stress, anxiety, heart rate and respiratory rate (Johansson K, 1999, Williams AF, 2002, Williams A, 2010).

For the effects described above, DLM combined with compression therapy is useful in lipedema for the management of pain and when it is associated with other pathologies such as lymphedema, orthostatic edema or venous insufficiency.

Even some patients feel psychological benefits produced by relaxation and report improvement in their quality of life (Ekici G, 2009, Hammer JB, 2007, Kim SJ, 2009, Szolnoky G, 2008, Todd M, 2016, Weiss JM, 2002). We found evidence on pain reduction (Level 1c) and on improving physical function (Level 4c) (Haesler E, 2016).

The DLM is not the treatment of choice in a "pure" lipedema, since the application of it will never decrease the fat and will not modify the volume or shape of the lower limbs.

This therapy is offered many times creating false expectations; However, the benefits obtained by patients with associated pathologies are important, especially in the reduction of pain, as reflected in the articles cited above.

They are **contraindications of DLM**: acute infections, signs of failure or decompensation of congestive heart failure, suspicion of concomitant malignant disease or tumor recurrence. The latter is not entirely consensual, the most recent studies seem to rule out that it increases the possibility of dissemination of the disease (Godette K, 2006). The treatment of obesity, as well as the correction of other aggravating factors such as osteoarticular alterations and poor plantar support, should be addressed simultaneously to the TDC.

KEY POINTS

- TDC and DLM are not indicated to reduce limb volume in lipedema when it is not associated with edema.
- The DLM associated with compression therapy can improve capillary fragility, reduce pain and discomfort of patients.
- TDC is useful when there is a lymphatic component associated with lipedema.
- The treatment of obesity, as well as the correction of other aggravating factors such as osteoarticular alterations and poor plantar support, should be addressed prior or simultaneously to the TDC.

PHYSICAL ACTIVITY, PHYSICAL EXERCISE AND SPORT

One of the most important recommendations for maintaining an adequate state of health is physical activity, but in patients with lipedema it is also required an accurate indication about how to perform and dosage of exercise physical, or practice a sport, whose purpose can be fun or competition.

The areas affected by lipedema do not reduce their volume with physical exercise, although this does help maintain weight and improve the quality of life of patients (Salmon P, 2001, Penedo, FJ, 2005, Todd M, 2016; Society of Lymphology, 2013; Fetzer A, 2015).

There is controversy regarding the indication and benefits of physical exercise in lipedema. The current evidence is in many cases clinical, there is no unanimity of criteria, thus manifesting the need for more scientific studies in this field.

It would be desirable for patients to achieve the following objectives:

- Improve overall health, self-esteem and quality of life.
- Keep your weight. If there is overweight, it must also be associated with diet. It is important to emphasize that the patient without an appropriate diet will not lose weight or fat only with exercise.
- Gain strength and muscular resistance, principally in lower extremities and favors mobility
- To prevent circulatory problems, articular and muscular

To achieve the proposed goals, it is recommended:

- Perform aerobic exercise, progressively and with low or moderate impact. High intensity or high impact exercises and contact sports are not usually the most beneficial; they can worsen the signs and symptoms of joint degeneration and pain.
- Practice sports in moderation. A priori there is none contraindicated.
- Do not perform sports that increase pain or bruising (such as contact sports).
- Perform a type of training that involves cardiovascular work.
- Try to activate large muscle groups. It is more advisable to work in isolated groups. That is, doing exercises that involve the contraction of as many muscles as possible, for example "squats" better than just doing a knee flexion.
- Train in company (Irwin BC, 2012). It has been shown that people who exercise with another person do it better and increase adherence. Being able to increase confidence due to problems related to self-image and other psychological aspects.

As for the need to wear compression garments during the exercise, there is currently controversy. More studies are needed to ensure the advantage of using them, given that some patients report that they restrict their movement, or they find it uncomfortable during the exercise (Cormie P, 2013) and the evidence of their benefit is low.

Despite this, most experts still consider that it is advisable to take them, especially if there is associated edema, and may withdraw if they hinder the exercise, explaining well to patients, the need to put them at the end of physical activity and for the rest of the year. day.

Some practical recommendations to carry out:

- **Walk or practice Nordic walking.** There are several studies that justify greater benefits of Nordic walking than just walking, since it increases the speed of walking and, as a result, generates the benefits of walking and adds more cardiovascular work, accelerates metabolism, improves movement, flexibility, strength, and endurance (Church SC, 2002, Porcari JP, 1997, Schiffer T, 2006, Takeshima MM, 2013, Tschentscher M, 2013).

In obese women, Nordic walking raises the intensity of exercise and adherence to the training program without increasing the perception of effort (Figard-Fabre H, 2011). We can affirm, therefore, it is more effective to walk with canes properly using the technique. There are more and more studies that support the benefits of Nordic walking in different pathologies such as intermittent claudication, heart disease, fibromyalgia, Parkinson's, sports injuries, and / or chronic back pain.

- **Functional exercises.** They improve tone and strengthen the trunk and limbs in untrained people. Such as hypopressive abdominal gymnastics, Pilates and body awareness exercises, proprioception circuits in stable and unstable planes, functional work with the own weight and with external resistances. It is desirable to obtain a muscular balance of 3/5 (in the scale of Daniels, a grade 3 corresponds to the ability to perform the movement in its full joint range and against gravity) and are suitable for the preparation of other sports practices.

- **Exercise in the water.** Activities such as aquagym, walking in the pool, swimming, using resistance materials or assistance with movement with fins. The physical properties of water reduce joint stress and pain, increase cardiovascular work and strength and promote mobility (Baum G, 1998, Tsourlou T, 2006, Grosse SJ, 2009, Petrick M, 2001, Sevimli D, 2015; Volaklis K, 2007).

Patients with associated circulatory problems (lymphedema, venous insufficiency), exercises in the water and their own immersion generate a feeling of lightness and freedom due to the stimulation of the venous and lymphatic circulation by hydrostatic pressure (Di Prampero PE, 1986). In addition, if they practice it on a regular basis, they achieve a reduction in pain, as indicated in the Consensus of the International Society of Lymphology, 2013.

- **Bicycle** (static or walking or mountain). The sitting position unloads weight to the lower extremities facilitating movement without joint stress. Increases cardiovascular work, helps the muscular development of the trunk and legs, increases balance, resistance and bone density (Oja P, 2011).

- **Sports such as yoga, Pilates and other similar** that combine different forms of muscular work directed, controlled and coordinated with breathing (Hagner-Derengowska M, 2015). These disciplines share the principles of strength work and elongation muscle, as well as concentration and body-mind connection. Therefore, in addition to the physical benefit, they influence the psychological aspect generating a sense of well-being.

All the exercises governed by different types / breathing patterns are carried out, facilitating exercise, protecting structures and preventing injuries and increasing concentration. Deep breathing in isolation is also recommended, as it increases the concentration of oxygen reaching the tissues and increases lymphatic flow, helping the possible loss of limb volume when there is lymphostasis (Mortimer PS, 1990; Todd M, 2016).

The results of the reviews of the exercise regarding the decrease in BMI are controversial, but there is a coincidence of positive results in studies conducted in sedentary women. Mazzarino M (2015) shows that the Pilates method can reduce pain, improve quality of life and resistance of the lower extremities.

With respect to yoga, although there are publications that mention benefits in patients with overweight and abdominal adiposity (Cramer H, 2016), in a systematic review carried out by Lauche R (2016) no positive effects on weight loss were found; body mass index, percentage of body fat or waist circumference.

KEY POINTS

- The indication of physical exercise in lipedema and the benefits that it entails are controversial.
- More scientific studies are needed on the practice of physical exercise, given that, although there is clinical evidence of its benefit, there is no unanimity of criteria.
- Physical activity in lipedema improves the quality of life and the self-esteem of the patients.
- It allows to gain strength and muscular resistance and to favor mobility.
- It contributes to prevent circulatory, joint, and muscular alterations.
- Physical exercise without a proper diet is not enough to lose weight or fat.
- Physical exercise does not reduce the volume of the lower extremities with lipedema.

NON-SURGICAL TECHNIQUES FOR THE TREATMENT OF BODY CONTOUR

These are techniques commonly used in the field of aesthetic medicine and can be applied in patients carrying pure lipedema or when they are associated with overweight / obesity, PEFE, localized adiposity, symptoms of heaviness of the limbs, orthostatic edema or chronic venous edema.

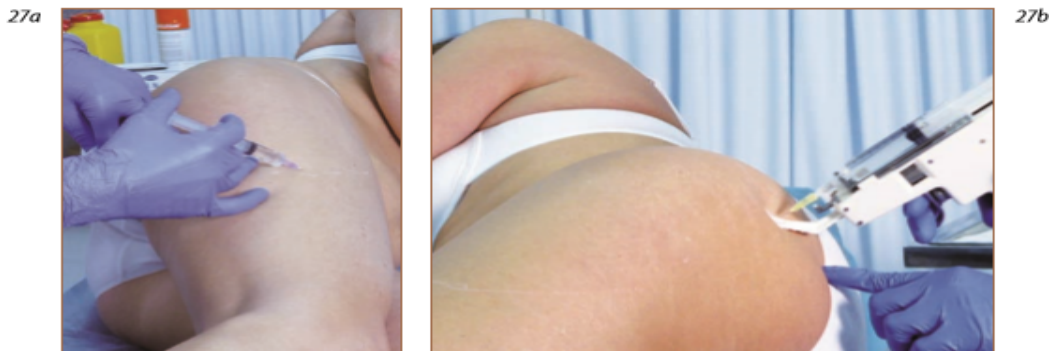
These techniques include the use of physical therapies or infiltration techniques such as mesotherapy / intradermotherapy or subcutaneous infiltration of substances with an adipocyte effect.

MESOTHERAPY / INTRADERMOTHERAPY

Mesotherapy as a medical technique was developed in Europe in 1952 by the French doctor Dr Michel Pistor. Its initial indication was the treatment of pain and circulatory disorders through loco procaine infiltration. From the 70s several studies were conducted that allowed to know a specific pharmacokinetics of the intradermal route (Herreros FO, 2011) Until the twentieth century was considered an empirical technique, but subsequent studies demonstrated the pharmacokinetic characteristics of this pathway. (Ordiz García I, 2016)

The term mesotherapy according to Ordiz García (2012) is defined as: "the therapeutic action that is obtained by acting on the superficial papillary dermis (derived from the mesoderm), which causes a double effect: pharmacological, dependent of the medicine and mechanical-reflex, dependent on the action of the needle "

More recently, the Italian Society of Mesotherapy proposes a Consensus to establish a series of recommendations in what they call "intradermal therapy" or "intradermotherapy", noting that despite the therapeutic benefits, more work should be done (Mammucari M, 2011). At present, the term intradermotherapy is considered more appropriate. It can be carried out by manual technique or by the use of electronic devices (assisted mesotherapy or "mesotherapy guns") (Fig. 27).



Figuras 27a y 27b. Técnica de infiltración (mesoterapia/intradermotherapia). Técnica manual (27a) y asistida (27b).

It is a medical procedure widely used in Aesthetic Medicine, and also in other medical areas such as traumatology, rehabilitation, rheumatology, sports medicine or dermatology, although there are no scientific studies to validate the technique and its indication in pictures clinical conditions as different as alopecia or pain treatment.

The indications of mesotherapy / intradermotherapy in the treatment of aesthetic pathology of the lower limbs are: PEFE in all its stages, associated with weight loss treatments; treatment of localized adiposities; complementary treatment of edemas of chronic or idiopathic venous cause, and tired legs.

In lipedema, it causes temporary improvement of the symptoms of pain and heaviness of the limbs, but without volume reduction. Obviously more studies are needed to validate this technique.

INFILTRATION TECHNIQUES OF THE SUPERFICIAL ADIPOSE PENCIL (sodium deoxycholate, hypoosmolar hydrolipoclasia):

Other infiltration techniques for the treatment of localized fat are the use of solutions such as sodium deoxycholate or hypoosmolar substances (hypoosmolar hydrolipoclasia). Its best indication is the treatment of the adipose panniculus with a thickness greater than or equal to 1.5 cm. Sodium deoxycholate acts causing panniculitis and fat necrosis, while hydrolipoclasia causes lipolysis. Unlike mesotherapy / intradermotherapy techniques should infiltrate to a depth greater than 6 mm.

Although these are techniques commonly used in the field of aesthetic medicine for the treatment of adiposities located in the abdomen, flanks, hips and knees, there are no published works on their indication and safety in the treatment of lipedema.

CARBOXYTHERAPY

Carboxytherapy consists in the subcutaneous or intradermal administration of carbon dioxide (CO₂). Its most known effects are: capillary vasodilatation; decrease in the affinity of hemoglobin for oxygen, which is more easily transferred to tissues, and activation of β adrenergic receptors in the adipocyte with lipolytic action.

Carboxytherapy is a technique commonly used in aesthetic medicine in the treatment of changes in body contour such as skin flaccidity in thighs, arms and abdomen; localized adiposities, and PEFE in all its stages. There are no references to its application in the treatment of lipedema, although in the PEFE it reduces localized fat, especially at the level of the thighs and hips and improves the "orange peel" (Georgia SK, 2010).

Its adverse effects are inherent to the treatment itself; Among them is pain or burning sensation, subcutaneous emphysema, and ecchymoses. CO₂ lacks toxic effects, and is metabolized by pulmonary and renal. Its safety profile is very high, since, due to its high solubility, it has little risk of embolization.

The usual doses used in aesthetic medicine (30 to 50 ml / minute / session), are easily compensated by a slight hyperventilation and there is no hypercapnia or acidosis in normal subjects.

ULTRASOUND (US). WAVES OF SHOCK

The twentieth century, led to the application of various techniques of physical medicine (use of currents or electrotherapy, iontophoresis, ultrasound) that is maintained and even increases in the XXI century developing new applications and extending the use of some of them (ultrasound, radiofrequency) to the medical field. Most of these techniques come from their use in physiotherapy and rehabilitation.

While the thermal effect dominates in high-frequency US (1 to 3 MHz), which are frequently used in physiotherapy, low-frequency US (30 to 50 Hz), also called cavitation, usually have a

dominant mechanical effect and they act in greater depth. Experimental studies show that ultrasound of low and high frequency have a double action on adipose tissue: lipolytic (Silva Gonçalves WL, 2009, Miwa H, 2002, Insua Nipoti E, 2013) and stromal compaction (Insua Nipoti E, 2013).

There are no specific works in lipedema, but reduction of the thickness of the adipose panniculus and improvement of the "orange peel" at the localized bitrocanthial and abdominal fat level has been observed (Insua Nipoti E, 2013).

Shockwaves are sound waves (ultrasounds) characterized by high pressure amplitudes relative to the ambient pressure; these waves move through the medium producing pressure differences extremes and temperature increase. The sound waves to be used for medical purposes are generated by extra corporal route and are introduced into the body without affecting the skin since the propagation of the acoustic waves is carried out according to the laws of acoustics-optics.

The use of shock waves is indicated in the treatment of kidney stones and various bone and soft tissue pathologies of the locomotor system. They are contraindicated in skin infections, bone tumors, metastases, pacemakers, pregnancy, children in the growth phase and coagulopathies. Since 2005 they have begun to be used in Aesthetic Medicine with effects at the level of flaccidity, PEFE and localized adiposities (Russe-Wilflingseder K, 2013).

The shock waves cause hyperemization by a vasodilator effect, at muscular level they favor the formation of the ATP (adenosine) that stimulates the neoformation of muscular fibers and reinforces the musculature, diminishing the muscular flaccidity. Also, an effect of stimulation of lipolysis has been attributed to them, although the latter is not proven.

Siems W (2005) demonstrates in his work that the use of shock waves would reduce the oxidative stress measured by blood parameters in patients with lipedema and / or PEFE. However, we have not found any subsequent studies or validated protocols for its use in lipedema, so there would be a lack of further studies to assess its efficacy.

ELECTROMAGNETIC RADIATIONS (EM): LASER, RADIO FREQUENCY, INFRA-ROJOS

Radiation is a source of energy that is transmitted through space, without requiring a direct contact between the source of emission and the area applied. The radiations produce an electromagnetic field around them and are able to penetrate the tissues causing a thermal effect. The electromagnetic radiation applied in aesthetics are: radiofrequency, infrared (with thermal effect on the surface that produces a vasodilatation and increased microcirculatory flow) and lasers. These techniques are used in the field of Aesthetic Medicine for the treatment of body contour alterations such as PEFE, flaccidity, localized adiposities or those associated with weight loss treatments.

Recently, so-called "low-level laser therapy" (LLLT) therapies have been incorporated for the treatment of localized adiposities (Gold MH, 2011, Jackson RF, 2013), but no protocol is

available for lipedema. . However, LLLT therapy could be indicated in lipedema because it is a "cold" laser whose purpose is bio stimulation and tissue biomodulation. Although studies that support this therapy are necessary.

It should be noted that within percutaneous laser therapy (not associated with liposuction techniques), a laser has recently been developed that produces localized heat at the level of superficial fat and approved by the FDA for the treatment of localized adiposities (Decorato JW , 2017). Due to its characteristics, this technique would be contraindicated in lipedema when venous and / or lymphatic insufficiency coexists.

The same happens with radiofrequency or infrared because they cause local caloric effects. However, this type of technique is indicated in the treatment of localized adiposities, especially in the gluteal region of the femur and improves the appearance of the "orange peel" (Goldberg DJ, 2008, Van Der Lugt C, 2009; Almeida M, 2014).

PRESSOTHERAPY

Negative pressure devices have an accessory (suction cups or rollers) that are connected to a vacuum producing mechanism. They are effective in all stages of PEFE where improvement of the "orange peel", smoothing of the skin and reduction of the thickness of localized fat is observed, especially at the bitrocanthereal level.

The positive pressure devices (intermittent pneumatic pressure therapy) use a compressor that introduces air at a certain pressure into compartments specially designed to adapt to the limbs. The most commonly used are multi-compartment pneumatic boots that allow the progression of the pressure cyclically from distal to proximal (Fig. 28).



fig 28

Positive pressure therapy acts at the venous and interstitial compartment, facilitating venous return and fluid drainage. It does not drain the accumulated proteins in the interstitium and neither has an effect on the fatty tissue been demonstrated, therefore there is no indication in lipedema except that it is associated with venous and / or lymphatic edema.

Its main indications are: chronic venous edema and postoperative edema. It has been suggested that it favors the reabsorption of postoperative hematomas and edema (post liposuction) (Zaleska M, 2015, Chardonneau JM, 2007).

It is contraindicated in the presence of neoplastic lesions, infectious processes, cutaneous trophic lesions, deep venous thrombosis in its acute stage, edema of systemic cause and should be used with caution in uncontrolled hypertensive patients.

THERMOTHERAPY / CRYOTHERAPY TECHNIQUES

They consist in the application of cold and / or heat for the treatment of body contour alterations.

Thermotherapy, application of heat: The application of local heat is used in the complementary treatment of overweight, fibrous PEFE and localized adiposity.

The heat applications in aesthetics include: use of creams with caloric effect, saunas, sweat bags, paraffin, ultrasound, infrared, electrotherapy and thermal hydrotherapy.

Due to its caloric effect, these therapies would be contraindicated in venous and / or lymphatic alterations, as well as in lipedema since the heat can worsen the symptoms.

Cryotherapy or cold application: the application of cold or cryotherapy is used in treatments of chronic venous edema, tired legs, PEFE and flaccidity; uses substances that lower skin temperature through contact with it (gels, cold bandages, cold baths, etc.) and should be differentiated from other techniques that use cold such as cryolipolysis aimed at the treatment of localized adiposities.

The criolipolysis uses equipment composed of a suction system that maintains the adjusted temperature below 0° C throughout the application. After approval by the FDA for the treatment of adiposities located on the flanks (Manstein D, 2008, Coleman SR, 2009) new applications have been emerging in localized abdomen and jowl fat, but we do not know its use in lipedema.

KEY POINTS

- There are no prospective studies that compare the results of different non-surgical techniques in reducing the thickness of the adipose panniculus and improving the orange peel skin.
- Most of the publications refer to the treatment of PEFE and adiposity located at the abdominal, flank and gluteal-femoral regions with improvement in volume and "orange peel", although there is no evidence of scientific evidence.
- There are no publications on the use of mesotherapy / intradermotherapy in the treatment of lipedema. Although clinical practice guides the improvement of pain without changes in volume, scientific studies are needed that can validate this technique.
- The application of non-invasive techniques with lipolytic purpose and stromal improvement could occupy a place in the therapeutic protocols of lipedema although the experiences of the

members of this Group agree that most of these techniques improve the pain of the extremities, but with little reduction in the volume of the members.

■ The purpose of non-surgical treatments is the improvement of the body contour and although they do not offer definitive results, they are a good complement to the slimming techniques.

CH. 6 TRATAMIENTO QUIRURGICO

The surgical treatment of lipedema has become, in the last decade, the only definitive treatment option for these patients, present in clinical guidelines and protocols and must be performed by plastic surgeons. Its main objective is the reduction of the fatty compartment by reducing the circumference and volume of the extremities.

The surgical treatment of lipedema can be carried out at any time, being especially indicated in those patients who do not respond adequately to conservative treatment (Schmeller W, 2014).

LIPOSUCTION

It is the least invasive method to eliminate subcutaneous fatty tissue, being the choice in those patients without comorbidity and who do not respond to conservative treatment. (Schmeller W, 2014, Dadras M, 2017) (Figure 29).

The results obtained in the longitudinal study carried out by Dadras M (2017), corroborate the results of authors such as Rapprich S, (2011), Schmeller W, (2012) and the recent long-term study of Baumgartner A (2016) demonstrating that liposuction is a safe and effective treatment for lipedema with good long-term results and few complications.



The weight should be normalized before proceeding to the surgery and it is important to achieve adherence to conservative treatment, since it is not appropriate to pose a liposuction to the patient if she is not willing to follow a correct pre and postoperative treatment.

Prior to surgical treatment, associated aggravating factors such as edema, obesity, unhealthy lifestyle or lack of physical activity should be corrected.

TYPES OF LIPOSUCTION

1. **Tumescent:** a solution containing saline, anesthetic and adrenaline is injected into the subcutaneous space to turn the area into tumescent. The serum produces a hydrodissection

separating the fat cells from the connective tissue septa. Adrenaline reduces bleeding. (Figure 30).

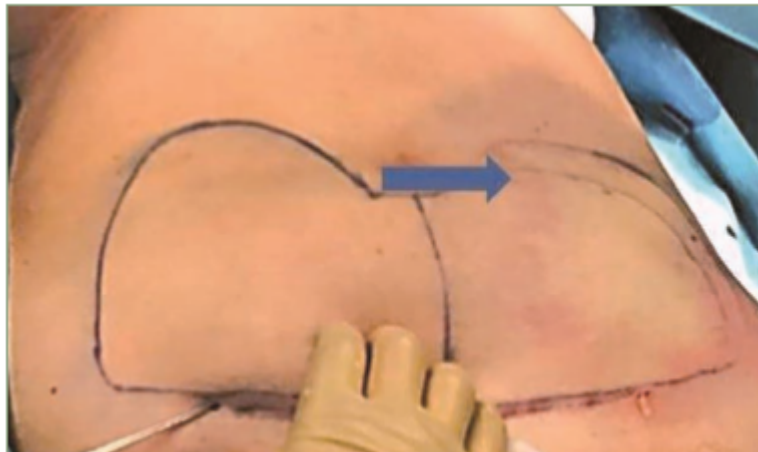
2. **Supratumescent:** greater amount of solution is injected in the subcutaneous space.

3. **Water Assisted (WAL, Water Assisted Liposuction):** the amount of solution introduced is less. It is performed through a modified cannula, which allows to inject solution simultaneously with the aspiration and directly separate the fat cells from the connective tissue, while aspirating (Stutz J, 2009).

4. **Vibro-Liposuction:** Power assisted liposuction is a type of liposuction in which a vibrating cannula is used. Invented by Malak, it was called vibro-liposuction. (Rebelo, A., 2006) The use of vibro-liposuction associated with supratumescent infiltration is a safe and effective method in the treatment of lipedema. (Schmeller W, 2006, Klein JA, 1987, Illouz, YG, 1989, Sattler G, 2002, Habbema L, 2009, Fife CE, 2010, Forner-Lamb I, 2012, Rapprich S, 2011).

Any of the before mentioned can be used in the treatment of lipedema (Hoffmann JN, 2004).

Liposuction with laser or ultrasound produces heat, and therefore, these techniques should be avoided, since there is an increased risk of concomitant lymphatic injury.



LIPOSUCTION TECHNIQUES

In liposuction, small incisions are made in the skin for the introduction of the cannula. These incisions are 2-4 mm and are performed in the most appropriate locations for the removal of fat.

The liposuction technique in lipedema is different from conventional techniques. Thinner and blunt cannulas are used, and liposuction must follow an axial or longitudinal pattern, and not transverse as usual in traditional liposuction. The objective is to minimize the potential lesions of the superficial lymphatic system (Mladick R, 1990).

The perfect anatomical knowledge and the correct execution of the technique are essential to reduce the possibility of complications, in specific areas such as ankles and knees (Frick A, 1999).

It is a sequential treatment, because to achieve satisfactory results and maintain safety criteria, it is necessary to perform an average of 2 or 3 interventions, with a variable range between 1 and 6.

RESULTS

With liposuction in lipedema, not only reduces the volume of fat in the affected areas (Rapprich S, 2011), but also reduces pain, spontaneous bruising, and edema, decreases sensitivity to pressure and improves the mobility, which leads to a better quality of life.

These changes are maintained in all parameters in the long term, as some studies already show (Schmeller W, 2012, 2014, Peled AW, 2012, Dadras M, 2017). However, it is necessary to perform postoperative care and maintain long-term controls such as maintaining weight, practicing physical exercise and healthy habits. Authors such as Schmeller W (2006 and 2012) also recommend maintaining conservative treatment.

It has been shown that liposuction using the tumescent technique is a safe and appropriate procedure in the treatment of lipedema (Habbema L, 2009).

It is important to be able to quantify these results in an objective way. The pre and post operative digital photographs can contribute to this. Methods such as ultrasound or MRI allow us to obtain measurable values. It is undeniable that, with the advent of new technologies, the increase in the resolution of ultrasound images and the development of more precise evaluation techniques, high resolution ultrasound has become a complementary diagnostic method. It is an effective, low cost method that allows us to assess changes in subcutaneous tissue thickness after surgery. (Whittle P, 2004).

The hormonal variations, changes in weight or discontinuity in the maintenance treatment can cause the new accumulation of fat in areas subject to liposuction.

DERMOLIPECTOMY

This surgical treatment involves the extirpation of large localized deposits of lipedematous tissue. These deposits cause severe mechanical difficulties, or even a complete inability to walk.

Despite the less invasive approach to liposuction, there are cases of significant mechanical limitations, in which excision by longitudinal excision may be the only treatment. (Miller TA, 1998, Wollina U, 2014).

In excisional dermolipectomy, the incisions are longer and significantly less cosmetic, with a higher probability of complications.

ASSESSMENT AND PREOPERATIVE TREATMENT

It is important to make an adequate selection of patients with lipedema before performing the surgical indication, to minimize the risks and achieve the best functional and aesthetic results.

In general, patients should undergo conservative treatment for 6 to 8 months, before undergoing surgical treatment (Dadras M, 2017), following the guidelines established in other clinical guidelines such as Lontok E (2017) although these care should be indicated individualized according to each case.

It is necessary prior to surgical treatment:

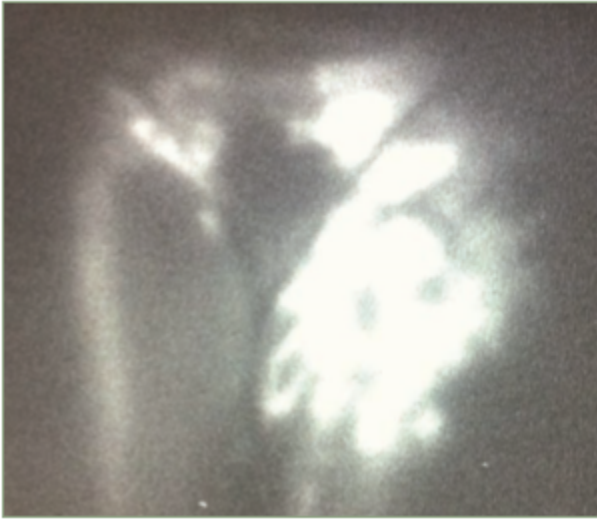
- Discard comorbidities that increase the anesthetic and operative risk
- Weight control, even if bariatric surgery is indicated in morbidly obese patients prior to liposuction and / or dermolipectomy (Coppel T, 2017)
- Get good emotional control. A balanced psychological and mental state is essential before indicating surgical treatment since they are long processes, which often require several surgical interventions.
- Analysis of skin characteristics to explain the possible need for post-liposuction surgeries to remove excess skin tissue.
- Commitment on the part of the patient to use the compression garments during the postoperative period.
- Create realistic expectations regarding possible outcomes

The following tests prior to surgery are recommended:

- Measures of the affected limbs (perimetry ANNEX 2).
- Ultrasound
- Visual analog scale for pain (ANNEX IV).
- Body mass index (BMI).
- Registration of the activity (METS, ANNEX VI).
- SF36 quality of life scale (ANNEX V).
- Lymphoscintigraphy (LGG)
- Lymphography with green indocyanine: used to visualize the superficial lymphatic system. For its realization, 0.2 ml of intradermal indocyanine green contrast between the digital commissures is injected. The lymphatic distribution pattern is visualized through a camera. It is the most sensitive test for the early detection of lymphatic alterations (Burnier P, 2017). The

dermal extravasation of contrast is a sign of alteration of the superficial lymphatic system (Figure 31.).

It is important to confirm the presence or absence of the lymphedematous component. (Buck DW, 2016, Warren Peled A, 2016) since the results obtained may vary, especially if a specific postoperative treatment regimen is not continued in case of lymphedema coexisting. The presence of lymphedema is not a contraindication to perform liposuction, but the long-term results are more uncertain. In this group of patients, the post-operative TDC is of special importance.



POSTOPERATIVE CARE

During the first 4 to 5 days after surgery it is not uncommon for patients to require walking crutches.

For at least 6 weeks they should wear a circular compression garment. Subsequently, the most appropriate compression stockings for each patient will be prescribed individually. Compression stockings should be changed every 6 months (Halk AB, 2017, Reich-Schupke S, 2017).

From 1 week after surgery, rehabilitation treatment can begin, taking into account that early mobilization of the skin, can cause seroma, undesirable adhesions to underlying structures, skin folds and sagging. This treatment must be planned individually and according to the experience of each specific work group.

This SLN has not been able to reach a consensus on the systematic indication of DLM in the postoperative period of surgical treatment of lipedema, given that we have not found studies that validate postoperative protocols in lipedema and compare the results of groups with and without postoperative treatments.

The number and frequency of the DLM sessions have not been defined, but this GC considers that they will be established in a personalized manner.

After the intervention, it is advisable to take the tights 24 hours a day without interruption, for 3 weeks. Subsequently, the most appropriate compression garments will be prescribed for each patient and individually.

Postoperative swelling and pain may take several months to resolve. (Coppel T, 2017).

In the immediate postoperative period, patients should perform simple physical exercises: isometric exercises of the lower limbs to maintain muscle tone and improve venous return.

KEY POINTS

- Surgical treatment in lipedema is indicated in any case, especially if the patient does not improve with conservative treatment.
- It should be preceded by 6 to 8 months of conservative treatment, weight control and emotional balance.
- Liposuction in lipedema requires a specific technique and should be performed in specialized units
- Techniques such as tumescent, supratoumous or WAL (Water Assisted Liposuction) liposuction can be used, while laser-assisted or ultrasound-assisted liposuction should be avoided.
- Postoperative care must be planned individually by the surgeon and the team of specialized professionals.

CONCLUSION

Lipedema is a clinical entity of a chronic nature, typical of the female sex, with special involvement of the lower limbs, poorly known, underdiagnosed and often confused with lymphedema, lipodystrophies or obesity. It was originally described in 1940 but has regained relevance probably related to the conditioning factors of 21st century fashion, where stylized bodies are a claim for most women.

Most of the literature available in lipedema comes from vascular specialists, rehabilitators, lymphologists, physiotherapists or lymphedema treatment units, which causes a bias when it comes to knowing the true incidence of lipedema in the general population; therefore, the available epidemiological data are scarce and little useful to help us determine the exact incidence of it.

The etiology and pathophysiology of lipedema are not sufficiently clear.

The diagnosis is fundamentally clinical, since specific diagnostic tests are lacking or that are supported by sufficient scientific evidence. However, its clinic may imply a deterioration in the quality of life of patients, due to the physical, psychological and social impact that it entails. As soon as this Consensus Document comes to light, lipedema is not considered a disease by the WHO, although a revision of the ICD 10 (which will be followed by the ICD 11) will be final on May of 2018, and which includes other proposals such as the consideration of "lipoedema" and "cellulitis" (PEFE) within the pathology of fatty tissue. <https://icd.who.int/dev11/f/en>

In this context are added the publications of the last decade in the field of plastic surgery that propose as an alternative to conservative therapies, the surgical treatment of lipedema. The most recent studies show that the technique is safe and can be indicated in selected patients, but to date there are no agreed protocols on pre and postoperative requirements and care, as well as controlled studies that validate the different proposed liposuction techniques (tumescent , supratumescente, WAL, vibro-liposuction).

For all this, the Consensus Group wishes to reflect the complexity of the approach to lipedema as well as the difficulty in obtaining a unanimous opinion in all the sections, although we have been able to bring opinions in most of the Chapters that have been reflected in Key Points, although new studies leading to a Clinical Practice Guideline will be necessary.

We highlight the following conclusions

- Need to establish if it is a disease or an aesthetic alteration. At the time of publication of this Consensus Document, the World Health Organization (WHO) does not consider lipedema as a disease, although we are aware of the proposed revision of the ICD-11 Beta Draft, according to which lipedema it would be included within the group EE82 (non-inflammatory subcutaneous fat disorders, EE82.2: Lipoedema) together with symptoms such as subcutaneous lipomatosis (EE82.3) or cellulitis (EE82.3) among others.

This group of experts considers that lipedema, when it is not associated with diseases or aggravating circumstances (obesity, venous or lymphatic insufficiency, osteoarticular alterations, immobility, etc.), may not meet all criteria to be considered a disease. Given that currently there are no diagnostic criteria agreed upon and accepted by the scientific community to confirm the presence of lipedema, further studies and lines of research are necessary to establish whether this entity meets the criteria of disease or is an aesthetic alteration that it causes psychological and social distress to those who suffer from it.

- **Definition.** The term itself, "lipedema" is not very accurate and gives rise to confusion, since there is no true edema in all cases, in the case of a fatty tissue pathology as confirmed by diagnostic imaging techniques.
- **Epidemiology.** Current epidemiological data are insufficient and heterogeneous. Given that the diagnostic criteria are not standardized or agreed upon, the prevalence data vary from one publication to another, most of which come from clinics or lymphedema units, so the exact incidence of lipedema in the general population, is unknown. However, we have found that there is an increase in the demand for treatments of patients with lipedema in recent years, which has aroused growing interest in this clinical entity described in 1940.
- **Aesthetic requirements.** The fashion of the XXI Century requires stylized bodies, and this may have an influence on the rejection and / or isolation suffered by patients with lipedema.
- **Etiopathogenesis and physiopathology.** They are not well known and some of the proposed theories lack sufficient scientific evidence. This group considers the need to open new lines of research aimed at the study of adipose tissue to clarify whether the circulatory blood and lymphatic mechanisms described in the literature, participate in the etiopathogenesis of lipedema or coexist with it.
- **Diagnostic criteria.** It is necessary to reach a national and international consensus regarding the diagnostic criteria of lipedema and its aggravating factors. A high percentage of patients with lipedema present overweight / obesity or associated venous disease that worsen the clinical picture and aggravate the prognosis, so they must be properly identified and adequately treated.
- **Classification.** In the literature analyzed we found that lipedema is confused with morbid obesity, lipodystrophies, PEFE, localized adiposity and rare adipose tissue syndromes, and that this confusion extends to the current classifications, which complicates the diagnosis and follow-up of patients. For this reason, this consensus group considers the need to establish a new classification of lipedema that allows the validation of therapeutic results with scientific evidence.
- **Assistance demand. Treatment** Patients with lipedema come to different professionals, due to the disparity of signs and symptoms they present, such as pain in the lower extremities and increased volume of them. Given that there is currently no consensus on the most effective

treatment for lipedema, this type of patient should be treated in multidisciplinary units where an adequate diagnosis and treatment of lipedema and its aggravating factors is carried out.

Due to all this, this group raises the need to carry out new studies and open research lines that clarify these issues. However, we unanimously agreed that patients with lipedema should be treated by a multidisciplinary team to establish:

- **The true prevalence of lipedema in the Spanish general population**, for which we propose the possibility of conducting a survey that can be developed through inclusion of large groups of patients recruited through different specialties and with the joint support of the scientific societies involved. (LOOK AT ANNEX 1).
- **The correct diagnosis of lipedema** based on agreed criteria.
- **The diagnosis of overweight / obesity**, which should always be treated, while stimulating physical activity to the detriment of sedentary lifestyle. Patients with normal weight lipedema, who regularly practice physical exercise, improve their symptomatology, which indicates the importance of prevention.
- **Therapeutic protocols for pain**, using appropriate assessment scales to measure the results of the different therapies (SEE ANNEXES 3 and 4).
- **The analysis of the results of the different therapies, adequately defining their indications and the degree of scientific evidence.**
- **The assessment of the repercussions of lipedema in the psychosocial sphere and the quality of life of the patients, determining the need for specific therapies. (SEE ANNEX 5).**
- **The requirements for the selection of patients who will undergo surgical treatment**, validating the surgical techniques and the most appropriate pre and postoperative protocols.
- The promotion of the implementation of Multidisciplinary Units for the diagnostic and therapeutic approach of lipedema.

At this point, we can address some of the uncertainties raised in the introduction:

- **Is the pathophysiology currently described to explain the disease correct?**

This group agrees that the etiopathogenesis and pathophysiology of lipedema are not well known and some of the proposed theories lack sufficient scientific evidence.

- **Is it a progressive alteration? Does it always evolve towards deterioration?**

The clinical evolution of lipedema is not correctly described. This group considers that factors such as obesity, immobility, lymphatic and venous insufficiency are aggravating and non-etiotropic factors of lipedema. The term lipolymphedema is used in the literature to

define the association between lipedema and lymphedema. However, it is not clear that this association constitutes a clinical entity or an evolutive picture of lipedema.

- **Is it possible to lose weight?**

Overweight / obesity are frequently associated with lipedema and constitute an **aggravating factor** that worsens mobility, favors osteoarticular complications and affects the quality of life and self-esteem of patients. Although the fat of the lower half of the body does not respond to diet or physical exercise, it is essential in patients with lipedema to make an adequate diagnosis of overweight / obesity and to propose the appropriate dietary treatment. Patients with lipedema who remain in normal weight and usually perform physical activity have fewer symptoms, better functional capacity and fewer complications than those who do not. (Coppel T, 2017)

- **Is the progressive increase in the percentage of body fat due to lipedema normal?**

The lipedema is an alteration that increases the deposit of fat in the lower half of the body, causing a manifest disproportion with the upper half. The involvement of the lower limbs is bilateral and symmetrical, respecting the foot, originating the so-called "legs in stovepipes" or in "pantalo pants".

Lipedema can be found in women with normal weight, underweight or anorexic, although in more than 50% of cases it coexists with overweight or obesity. As it is an almost exclusive affectation of the feminine sex, we must remember that from the puberty the corporal fat represents approximately 25% in the woman and 15% in the man. In young women, the distribution of fat predominates in the hips (gynoid distribution), whereas with age the fatty tissue of the limbs decreases as the central location increases, this change is more evident in postmenopausal women. However, if excess fat coincides with an abnormal BMI, it should be considered overweight / obesity associated with lipedema.

- **If the main symptom is not edema: Is manual lymphatic drainage (MLD) an essential tool for treatment?**

As this group has agreed and according to a critical reading of the published literature, the increase in the volume of limbs in lipedema responds to the symmetric accumulation of adipose tissue and may or may not be associated with edema. The most common form is orthostatic edema, as originally described by Allen EV (1940), although there is an absence of fovea. Systemic, venous or lymphatic edemas can also be associated. In the case of associated lymphedema, it is not clear whether this is primary or secondary to the obesity present in most patients, nor the causal relationship between both pathologies. The use of complementary functional techniques and diagnostic imaging (lymphoscintigraphy, ultrasound, MRI) allows to determine if it is a "pure" lipedema or is associated with edema, in which case specific treatments should be established according to the etiopathogenesis of edema.

Coinciding with other authors, this working group considers that DLM is not the treatment of choice in an asymptomatic lipedema when you only want to reduce the volume of the limbs, since the application of this will never decrease the fat, so this treatment will be offered many times creating false expectations. However, it has been shown to produce symptomatic improvement, mainly in pain (level of evidence 1c (Haesler E, 2016) and psychological benefits and in the quality of life of patients (Weiss JM, 2002; Kim SJ, 2009; Todd M, 2016; Szolnoky G, 2008; Hamner JB, 2007; Ekici G, 2009) .

The DLM would be indicated when there is associated lymphedema, as a component of Complex Decongestive Therapy.

- **Is it correct to prescribe compression garments in all cases?** Not always. This group wishes to emphasize that compressive therapy is indicated in case of orthostatic edema / venous insufficiency and / or lymphedema associated with lipedema. It can also be used for its effects in the improvement of pain in lipedema, as well as for the support it confers tissue and its contribution to limb remodeling in some patients. Prescription must always be personalized
- What are the most effective treatments?

Given that, at present, the etiopathogenesis of lipedema is unknown, we lack an etiological treatment.

The different treatments analyzed are mainly directed to the control of the symptoms, to the reduction of the edema (when it exists) and to the remodeling and reduction of the volume of the extremities. Compressive therapy is an essential element in case of associated edema.

This group considers it essential to establish a diagnosis and adequate treatment of pathologies coexisting with lipedema, such as obesity, chronic venous disease, lymphoedema, osteoarticular alterations or immobility.

To be able to analyze and compare the results of different treatments with scientific criteria, it is necessary to have an adequate patient classification system, as well as assessment tools that allow measuring clinical changes.

In the field of aesthetic medicine, satisfactory results have been observed through hygienic-dietetic care and non-surgical techniques for the treatment of body contour, especially in localized adiposities and PEFE associated with lipedema, but future studies are necessary to be able to Establish your indications.

The normalization of weight and the usual practice of physical activity have an effective impact on improving symptoms and functional capacity, while reducing associated complications. The surgical treatment of lipedema has become in the last decade an alternative option to conservative treatment and its main objective is the reduction of subcutaneous fat, thus reducing the circumference and the volume of the extremities.

The surgical treatment of lipedema can be carried out at any time, being especially indicated in those patients who do not respond adequately to conservative treatment (Schmeller W, 2014).

It is important to emphasize that the therapeutic approach of lipedema is always multi and interdisciplinary.