
Lipoedema

CLINICAL REVIEW

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Lipoedema is a disease that affects women and is characterised by an abnormal accumulation of fatty tissue, with pain and a feeling of heaviness in the lower limbs. Approximately 30 % of patients also have involvement of the upper limbs. The cause of lipoedema is unknown, but familial clustering of the condition suggests an underlying genetic cause. Oestrogen and hormonal changes appear to be involved, as the condition occurs predominantly in women and is linked to hormonal fluctuations. In Norway, women with lipoedema have had limited access to treatment within the public health service, and the condition is relatively unknown among Norwegian healthcare personnel. Internationally, the diagnosis and treatment of lipoedema are largely based on consensus, as there is a lack of definitive scientific evidence in relation to pathophysiology and treatment. This clinical review presents lipoedema diagnostics and treatment based on clinical experience and international published consensus statements.

Lipoedema – the development of painful fatty tissue on the extremities – usually begins at puberty. The cause is unknown, but oestrogen and hormonal changes appear to be involved, as the condition primarily affects women and often worsens during pregnancy and menopause. A familial pattern is frequently observed (1, 2). The condition is not included in the ICD-10 classification system, and its prevalence in Norway is therefore unknown. The public health service in Norway has no standardised treatment provision for patients with lipoedema. Some regional health authorities have offered conservative treatment in the form of compression garments, while liposuction of painful fatty tissue has been offered sporadically, primarily in Northern Norway Regional Health Authority.

Lipoedema was identified in the 1940s (3), but there is still limited reliable scientific knowledge about its pathophysiology and treatment. The diagnosis is primarily descriptive and based on consensus, but discussions are ongoing. Due to poorly defined diagnostic criteria and a lack of epidemiological studies, prevalence estimates in the literature vary widely, from 1 in 72,000 (4) to 10–40 % (5). Internationally, there is discussion about whether pain in the fatty tissue should be a diagnostic criterion and whether pathological lymphatic drainage is present in lipoedema. In Europe, there is now consensus that the lipoedema diagnosis includes a pain criterion and that the lymphatic system is normal, whereas the US consensus does not require pain for diagnosis and considers lymphatic drainage in the fatty tissue to be pathological (1, 6). The

medical community in Norway follows the European consensus. The lack of knowledge about diagnosis and treatment poses challenges both for the women affected and for the health service.

This clinical overview presents lipoedema diagnostics and treatment based on European consensus-based guidelines (1), a non-systematic literature search and clinical experience from the ongoing national trial for the surgical treatment of lipoedema.

Clinical presentation and diagnostics

Lipoedema is a clinical diagnosis, and there is no diagnostic test or biomarker that confirms the condition (2). The onset of symptoms, symptom profile and family history are relevant factors in patients' medical history (4). Figure 1 illustrates the clinical signs of lipoedema.

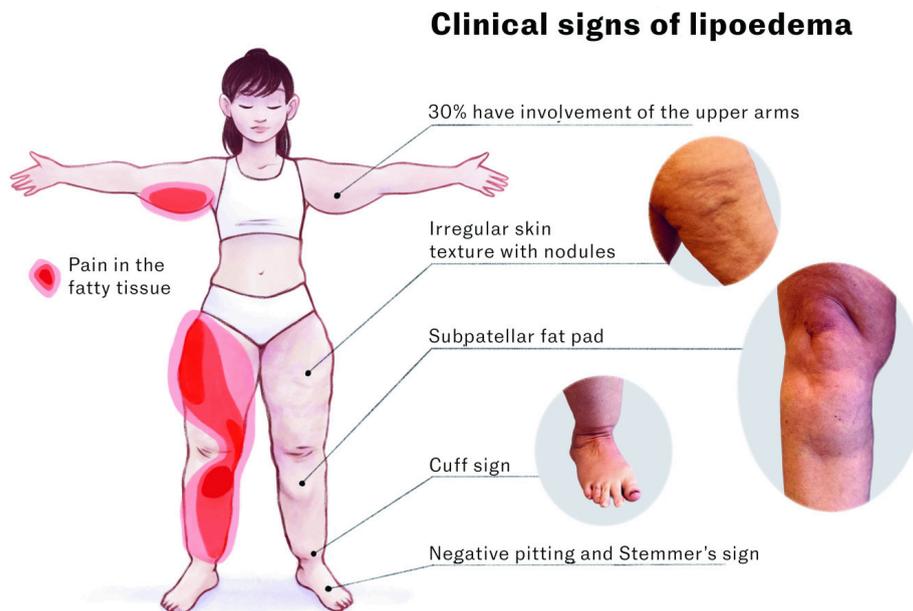


Figure 1 Clinical signs of lipoedema. The illustration shows the characteristic fat distribution and body shape seen in lipoedema (2, 6). The red shading indicates areas of pain, with darker shades representing greater pain intensity. The pitting test is performed by pressing the thumb firmly against the tissue for one minute; the test is considered positive if a visible indentation from displaced fluid remains. Stemmer's sign indicates fibrosis caused by lymphatic fluid in the tissue and is positive if the skin at the base of the toe cannot be properly pinched. Illustration by Karoline Forsund. Adapted by the Journal of the Norwegian Medical Association.

The most common symptoms of lipoedema are pain and a feeling of heaviness in the lower limbs. Patients with lipoedema have a disproportionately large amount of subcutaneous fat tissue on their thighs and lower legs, and sometimes the upper arms, compared to the rest of the body. The fatty tissue is symmetrically distributed, and the feet and hands are not affected. The condition is classified by type and stage based on clinical appearance. Type refers to the anatomical location, while stage describes the changes seen in the

skin and underlying fatty tissue as the volume increases (Figure 2) (2). Comorbid obesity leads to more voluminous lipoedema and can overload the lymphatic system, potentially resulting in secondary lymphoedema (4). Studies have shown a high prevalence of psychological issues in this patient group and that lipoedema negatively affects quality of life and mental health (7).

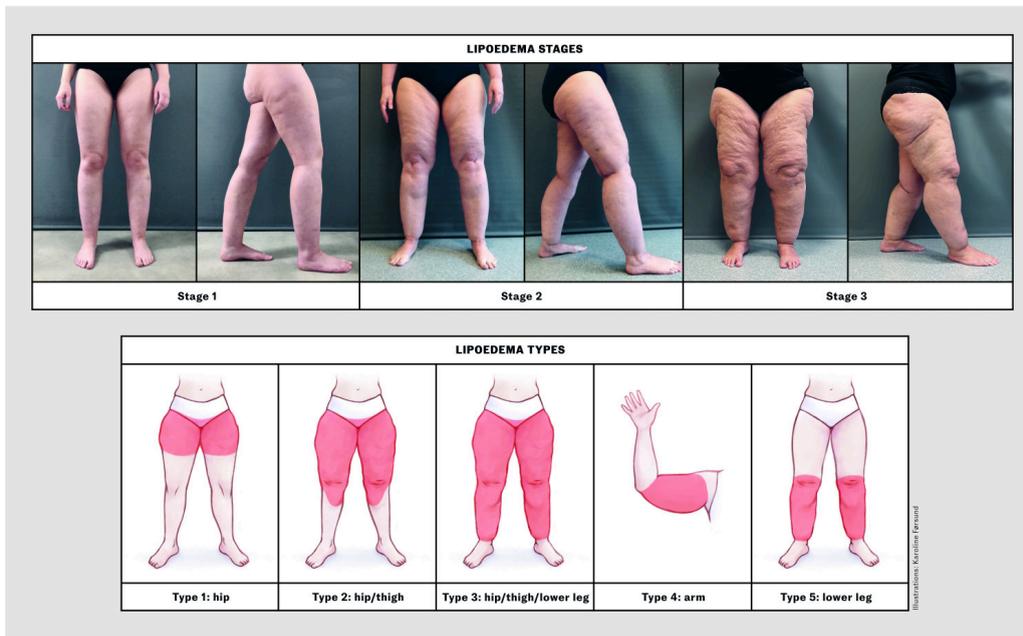


Figure 2 Lipoedema stages and types. The images in Figure 2a show changes in the skin surface and the texture of the subcutaneous tissue, which can also be identified through palpation. The skin changes in stages 1 to 3 are characterised by visible indentations and palpable nodules, increasing in size depending on the stage (2). The illustrations in Figure 2b show the different lipoedema types, which refer to anatomical location. It is not uncommon for a combination of types to occur (2).

The cause of the pain in lipoedema fat remains unclear. Hypotheses involving abnormal anatomy and metabolism, inflammation and hypoxia in the fatty tissue have not led to any confirmed pathophysiology (1, 2).

Differential diagnoses

Obesity is both a differential diagnosis and a common comorbidity in patients with lipoedema (1). Unlike obesity, lipoedema is characterised by a strikingly disproportionate fat distribution and significant pain in the fatty tissue (2).

Lipohypertrophy is characterised by disproportionate fat accumulation similar to lipoedema, but without pain in the fatty tissue.

Lymphoedema is caused by fluid accumulation in the tissue and differs from lipoedema in that it usually occurs unilaterally and involves the hands and feet. Lymphoedema typically also presents with pitting oedema and a positive Stemmer's sign (6).

Other rare adipose tissue disorders can also cause painful fat. In Dercum's disease, pain is also located in the fatty tissue, but the condition can affect the entire body and is often associated with lipomas (8). Fibromyalgia causes pain in more widespread areas of the body than just the extremities and does not involve distinct pain in the fatty tissue.

The diagnostic process is challenging, and the diagnosis should therefore be made by healthcare personnel who specialise in this area.

Treatment

The goal of treatment is to reduce pain and improve function and quality of life.

Conservative treatment

A multidisciplinary approach is recommended for the conservative treatment of lipoedema, which should include physical activity, compression therapy, psychosocial support, weight management, patient education and self-management guidance [\(1\)](#).

Physical activity improves circulation in the lower limbs, is generally beneficial to health and is one of the pillars of conservative lipoedema treatment [\(1\)](#).

Physiological orthostatic oedema can increase the pain associated with lipoedema. Compression garments can counteract this, help stabilise the fatty tissue and reduce discomfort during activity. Pneumatic compression and manual lymphatic drainage have been commonly used in the management of lipoedema and many patients report symptom relief [\(9\)](#). Based on the assumption that lipoedema is caused by pathological fatty tissue rather than pathological oedema, the effect of lymphatic drainage is uncertain beyond the reduction of orthostatic oedema. There is a lack of randomised trials investigating the efficacy of compression therapy. However, compression therapy remains necessary for overweight patients who have developed secondary lymphedema.

A high proportion of patients with lipoedema are overweight, and there is broad consensus in the medical community that weight gain exacerbates the symptoms. Weight management therefore plays a key role in treatment [\(1\)](#). Weight loss can reduce lipoedema-related pain. There is ongoing debate about whether a ketogenic diet may be particularly beneficial for this patient group [\(10\)](#), but randomised trials with adequate sample sizes are lacking. Our search in PubMed yielded no results for published works on the efficacy of GLP-1 analogues on lipoedema. Further research in this area is needed. With weight loss, whether achieved independently or through bariatric surgery, both lipoedema fat and other fat decrease in volume, but the disproportionality remains [\(11\)](#). In our clinical experience, many patients successfully lose weight, and sometimes symptoms are reduced to such an extent that they choose to forego liposuction. Weight loss also reduces the risk of developing secondary lymphedema and osteoarthritis.

Surgical treatment

Studies on surgical treatment for lipoedema have primarily focused on liposuction [\(12\)](#). Bariatric surgery may be considered in patients with comorbid obesity, but there is little research on its effect on lipoedema-related pain. Published research on bariatric surgery mainly focuses on lipoedema diagnosed

post-surgery (13). Following liposuction, significantly reduced pain, improved mobility and quality of life are reported, as well as a reduced need for further conservative treatment (14).

There are few studies on whether weight gain after surgical treatment for lipoedema leads to a recurrence of symptoms. Knowledge about the long-term outcomes of liposuction is also limited, but a published longitudinal study with data at 4, 8 and 12 years suggests that the pain-relieving effect persists despite weight gain (14). Based on our clinical experience, some patients do gain weight after surgery without the return of the characteristic lipoedema pain. However, many patients report increasing pain in untreated areas of the body, such as the upper arms, hips or lower abdomen. It is unclear whether this is due to residual pain being perceived as more intense once the competing pain is gone, or because weight gain is redistributed to new areas after the lipoedema fat in the legs is removed.

National and global treatment provision

In recent years, both European (1) and American (6) consensus statements on the diagnosis and treatment of lipoedema have been published. However, the treatment provision in the public health service is still lacking. Canadian health authorities have conducted a systematic literature review on the effectiveness of liposuction for lipoedema but point out that the studies have several limitations in terms of methodology, sample size and conflicts of interest (12).

Patients in Norway who have undergone liposuction have mostly paid for the procedure themselves through private healthcare providers. In 2019, the plastic surgery community in Norway submitted a report commissioned by the Ministry of Health and Care Services, recommending that surgical treatment for lipoedema be offered as a five-year clinical trial at one centre in each regional health authority (15). This led to the Surgical Treatment of Lipoedema trial in Norway, which is now in its fourth year. Over 200 otherwise healthy women with significant lipoedema-related pain and a BMI under 28 were randomised to receive either liposuction or compression therapy. A similar trial is underway in Germany (the LIPLEG trial) (16). These trials are expected to provide important scientific insights into the treatment of lipoedema.

The article has been peer-reviewed.

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