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Article

Lipedema: Clinical Pathology and Treatment

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Introduction:

Allen and Hines (1) first mentioned Lipoedema in medical literature in 1940. The disease is now fully recognised and listed in the WHO International Classification of Diseases (ICD) with its own number (E88.xx) (20). Multiple entries on the subject of lipoedema are now found in medical databases. The German Society of Phlebology has produced its own S1 guideline on this topic, published in a revised form in January 2024 (7).

The causes are not yet fully understood, but it is currently assumed that the female hormone oestrogen causes fat cells to multiply and enlarge through the increased release of growth factors (29, 30). The massive fat cell proliferation results in a lack of oxygen in the tissue, causing parts of the adipocytes to die off (31). This in turn triggers a chronic inflammatory process that leads to tissue damage.

Furthermore, there is an increased permeability of the vessel walls, so more lymphatic fluid leaks into the tissue. This can then no longer be removed by the intact lymphatic system (so-called high-volume insufficiency) and results in the typical feeling of pressure and tension (see below). Additionally the tissue environment changes, resulting in increased sensitivity of the pain receptors as the cause of the regularly presented spontaneous pain. Increased fragility of the blood capillaries results in a tendency to haematoma (35).

The prevalence in the female population is thought to be 8-17% (11, 18, 23). The disease also rarely affects men and is therefore usually associated with a hormonal disorder. However, there are currently only individual case reports (4, 10).

Symptoms and Diagnosis:

Coincidences often lead to a Lipedema diagnosis. Patients recognise their own symptoms for example in television reports or social media posts. Friends or acquaintances approach some patients about the strange appearance of their legs. Even though the disease has been known for over 80 years, knowledge and awareness of lipoedema is still very low in many places. The main symptom is pain (33). Initially, however, there is often only a profound feeling of heaviness. Pressure pain, painful to touch, spontaneous pain, tension pain, pain on movement or the initial feeling of heaviness can appear all together or independently of each other. There is also a tendency to haematoma without

adequate trauma (5, 28). The visual changes to the arms and legs naturally also contribute to the stigmatisation of patients.

In contrast to obesity, Lipedema never or hardly ever reacts to weight loss attempts (1, 13, 34). It presents bilaterally and symmetrically. Hands and feet typically stay slim. In the early stages, only the concave recesses next to the Achilles tendon may be filled (10); as the disease progresses, the typical columnar changes in the legs occur. Noticeable distinctions to the normal tissue form at the wrist and ankle joints. A clear fat collar ('fat muff') then appears here (Fig. 1). There is often an increase in fatty tissue medially below the knees. The Stemmer's sign (the skin of the second toe no longer wrinkles when lifted) is negative in contrast to lymphoedema or lipolymphoedema (13, 37, 42). In the late stage, the altered static and increased weight of the legs can lead to joint malalignment and osteoarthritis (Fig. 2) (39).

In the early stages, there is usually an increase and thickening of the fatty tissue on the upper arms; in later stages, heavily congested fat deposits form over the ulna and radius with a triangular recess on the flexor side of the wrist.

Depending on clinical presentation, lipedema is divided into 3 stages.

Stage 1: smooth skin
Stage 2: dimpled, irregular skin
Stage 3: dewlap formation, the skin shows large-volume pockets

Since 2024, staging classification is no longer listed in the current German guidelines and not used officially, as it did not provide any benefits in terms of a treatment recommendation.

The appearance of the skin alone determined the staging, which was not influenced by fat volume (7).

Fig. 1 Typical 'columnar' change in the legs, clear collar formation at the transition to the ankle joints

Fig. 2 Joint deformity (genu valgum) with long-standing lipedema

Currently no instrumental method can reliably detect lipedema. Sonography, magnetic resonance imaging or computerised tomography can only provide indications of increased or compacted fat deposits (22, 8, 25, 3, 27).
The actual diagnosis is made based on clinical criteria (21, 33). Even the histological analysis of diseased cells is unspecific, as demonstrated by Stutz in 2009 in 30 lipoedema patients after water-jet assisted liposuction (40). The process showed primarily intact lipocytes with low vascularisation. Whether the pathological growth of subcutaneous adipose tissue is adipocyte hypertrophy, hyperplasia or a combination of both remains unclear (33). In the meantime, research was expanded to include genetic and immunohistochemical analyses, but still have no findings that can be utilised in everyday life.
Clinical diagnosis is based on the patient's medical history with typical onset during puberty, pregnancy or the menopause (1, 43). There is often a positive family history, although the literature is still relatively variable with an incidence of 16-64% (1, 16, 38).
In 97% of cases, the legs are affected, in 31% the arms (19). From our own experience, however, we assume that the arms and legs are always affected equally. The manifestation on the arms is often less pronounced, or only becomes apparent later.

Treatment:
As with diagnostics, there are very few centres worldwide that specialise in the treatment of lipedema, particularly in surgical treatment. As a result, the quality of treatment results varies greatly. In order to achieve the best possible results, treatment in an experienced centre for lipedema is recommended.

For many years, complex physical decongestion using flat-knit compression garments and manual lymph drainage in addition to weight normalisation was the treatment of choice (12, 19, 41). Furthermore, intermittent compression can be carried out using home devices (‘Lymphomat’). These measures primarily serve to reduce oedema, but none of the methods mentioned can reduce the pathologically increased fatty tissue. Manual lymphatic drainage is currently not budgeted for the diagnosis of lipoedema and is therefore not subject to recourse assessment.
Although complex physical decongestion is recommended in the existing guidelines, there is no evidence-based study that proves its benefit (7, 41). Patients' quality of life is severely impaired by the lifelong need for tight-fitting compression garments and regular lymphatic drainage (9).
Liposuction has been used successfully in the treatment of lipedema since 2004 (23, 32).
So-called moist suction methods are used for treatment. Currently, the TLA (tumescent local anaesthesia) method and water-jet assisted liposuction (WAL) are used. Both methods show good results, but in our own clinic we see advantages in favour of WAL and therefore use this technique.
In order to work effectively and at the same time not jeopardise patient safety, the legs must undergo liposuction several times. As a rule, 2-3 liposuctions are required for the lower extremities, while the arms can normally be liposuctioned in one procedure. Overall, the complication rate of the procedure using a standardised surgical protocol is very low at 1-2% (36). The standardisation of the treatment enables optimal results for the patients (17, 44) (Fig. 3 and 4).
Multiple studies now confirm the effectiveness of liposuction for lipoedema. The Dutch guidelines state that abnormal fatty tissue in lipedema can only be treated surgically (15). In the S2k guidelines of the German Society of Phlebology, mention liposuction as a treatment option for every stage of lipedema (7).
Further studies confirm the benefits of liposuction and demonstrate a long-term effect (2, 5, 26, 36, 44, 45). To ensure the success of the treatment, weight normalisation is often necessary. For many patients, this requires a significant change

in lifestyle. The regulation of body weight through diet and physical activity is a decisive factor in the success of treatment.

In summary, all studies show a significant reduction in pain symptoms, on average by 70%. All studies to date are monocentric and not randomised. A multicentre prospective randomised trial (Lipleg study) is currently being conducted in Germany on behalf of the German government to test the benefits of liposuction for lipoedema. The first results are expected in 2025.

Liposuction for lipedema is not currently included in the health insurance catalogue of services in Germany and all other countries. An exception is stage 3 lipoedema, where the costs in Germany are covered by statutory health insurance under certain conditions (exhaustion of conservative therapy, BMI <35).

The quality of life of patients treated by liposuction is significantly improved. Frambach came to this conclusion in a study of 164 patients who were followed up on 4 and 8 years postoperatively (14). The pain symptoms were for the most part completely regressive over the entire follow-up period, as were the sensitivity to pressure, the tendency to oedema and the restriction of movement. Furthermore, there was no renewed increase in subcutaneous fat over the course of the treatment.

The current follow-up examination of our own patient collective confirms the good results and shows improvements of between 77% and 96% for the variables analysed (including pain, swelling, reduction in quality of life, reduction in ability to work) using water-jet assisted liposuction (44).

Last but not least, liposuction can end the lifelong dependence on compression garments and lymphatic drainage (36).

Fig. 3 Lipedema of the legs in stage 2 preoperatively

Fig. 4 After lipo-decompression of the legs, a total of 15 litres of pure fat in 3 operations

Summary:
Lipedema is a demographically significant disease and its pathological value is now well established. Liposuction is - irrespective of the assessment by health insurance companies - the only method to reduce the pathologically altered fatty tissue with maximum and lasting benefits for the affected patients.

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