



REVIEW ARTICLE

Lipedema—An update

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Abstract

Lipedema is a chronic disabling disease affecting the subcutaneous adipose tissue of the extremities in females during or after puberty. The disease is characterized by bilateral swelling of legs and/or arms, bruising, and pain. In contrast to lymphedema, the most distal parts remain unaffected. In contrast to obesity, patients with lipedema have a lower risk of diabetes mellitus. The pathogenesis is not well understood. However, hormonal factors seem to play a vital role, as it is an exclusively female disorder. The recent advantages in understanding and treating lipedema are reviewed.

KEYWORDS

bruising, complex decongestive therapy, edema, lipedema, liposuction, lymphedema, obesity, pain, subcutaneous adipose tissue

1 | INTRODUCTION

Lipedema is a chronic disease characterized by bilateral increased circumference of extremities, pain sensations, and bruising. It can be described as a painful lipodystrophy. The disease develops in females during or after puberty often in conjunction with sexual hormonal changes. It leads to a disproportionate body shape. In contrast to lymphedema, lipedema leaves the most distal parts, that is, hands and feet, unaffected (step-off sign or cuff sign) (Allen & Hines, 1940; Shavit, Wollina, & Alavi, 2018). The Stemmer sign is negative in lipedema (Wollina & Heinig, 2018). The skin is hypothermic and telangiectasias may develop later (Buck & Herbst, 2016).

Lipedema is often confused with obesity, as the BMI increases due to the swollen extremities. However, the adipose tissue in lipedema is resistant to exercise or diet.

The prevalence of lipedema has been estimated as high as 10% in adult Caucasian women (Marshall & Schwahn-Schreiber, 2011).

A symmetrical painless enlargement of subcutaneous adipose tissue of the extremities is characteristic for lipohypertrophy. As in lipedema, lipohypertrophy is seen in females only. It has a negative esthetic impact but misses the sufferings that are so characteristic of lipedema. The most common comorbidity in lipohypertrophy patients is obesity with 80% of affected patients (Herpertz, 2003).

The severity of lipedema is classified according to surface and structural changes in the adipose tissue (Stößenreuther, 2001; Table 1; Figure 1). This classification is limited as it does not consider volume of affected extremities, pain, BMI, nor impairment of mobility.

2 | COMPLAINTS AND QUALITY OF LIFE

In a recent Dutch survey, 163 patients with lipedema responded to various questionnaires related to quality of life issues (QoL). They reported the following complaints assorted by reported frequency: pain (88.3%), pain upon pressure (87.7%), easy bruising (85.9%), cold (71.8%), burning sensation (35.6%), and numbness (37.4%). There was not a single patient without complaints.

The most severely affected dimensions of QoL were physical limitations and pain compared to the Dutch average for females (Romeijn, de Rooij, Janssen, & Martens, 2018). These data shed a light on the most needed improvements warranted by any treatment for lipedema patients. The study also raises the question of lipedema-like conditions without pain. It seems that patients with lipohypertrophy have been included in this evaluation.

Lipedema has a negative impact on psychological well-being and self-esteem (Dudek, Białaszek, Ostaszewski, & Smidt, 2018), although the primary role of depression in lipedema has been questioned (Bertsch & Erbacher, 2018a).

3 | EDEMA

In early stages, lipedema is not characterized by a lymphatic insufficiency. In contrast, an increased lymphatic flow has been measured (Brauer & Weissleder, 2002). But does advanced lipedema lead to lymphedema?

TABLE 1 Classification of lipedema severity according to Stöbßenreuther (2001)

Stage	Skin surface	Subcutaneous adipose tissue
Stage I	Surface normal	Small nodules
Stage II	Surface uneven (peau d'orange)	Bigger nodules
Stage III	Lobular deformation	Large nodules and deformities

Lymphoscintigraphic evaluations of 83 patients with lipedema showed alterations in 47% of the patients, mostly of minor grade. None of the patients demonstrated more severe changes. There was no correlation to the following parameters: age, presence of Stemmer's sign, BMI, or clinical stage of lipedema (Forner-Cordero, Oliván-Sasot, Ruiz-Llorca, & Muñoz-Langa, 2018).

The tissue water content can be quantified by tissue dielectric constant (TDC) measurements. A 300-MHz electromagnetic wave is transmitted into the skin using a 2.5-mm depth probe. TDC calculated from the reflected wave is directly proportional to tissue water content ranging from 1 (vacuum) to 78.5 (pure water). Patients with lipedema had a TDC value in the range of healthy controls, that is, 0.5 ± 6.2 and 32.3 ± 5.7 , respectively (Birkballe, Jensen, Noerregaard, Gottrup, & Karlsmark, 2014).

The findings contradict the assumption that lymphatic or nonlymphatic edema is a significant factor for swelling of extremities in lipedema. They also argue against the concept, that lymphedema is a consequence of more severe lipedema (Bertsch & Erbacher, 2018b). These studies, however, excluded patients with lipolymphedema.

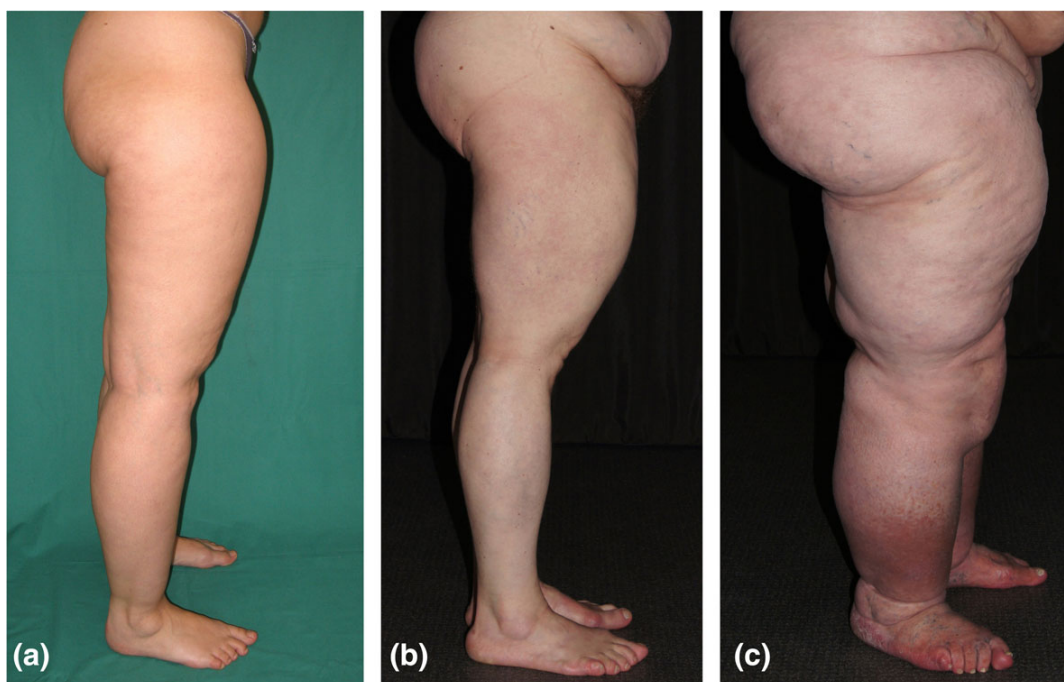
Lipedema patients may develop orthostatic edema due to a diminished and delayed arterio-venous reflex (Stöbßenreuther, 2001). Obese patients with lipedema are on risk for obesity-associated lymphedema and will benefit from weight reduction (Bertsch & Erbacher, 2018a, 2018b).

4 | ADIPOSE TISSUE

The body mass index (BMI) may be increased in lipedema patients without obesity. Objective measurements of body composition by dual energy X-ray absorptiometry (DXA) in lipedema patients demonstrated an increased adipose tissue mass of the legs (mean 0.82) adjusted to BMI and an increased mean leg trunk index of 0.70 (Dietzel, Reissauer, Jahr, Calafiore, & Armbrecht, 2015). That translates into a disproportionate adipose tissue distribution on legs (and arms) in contrast to obesity, where the trunk is mostly affected ("central obesity").

Is high-resolution sonography capable to ensure a reliable and reproducible differentiation of lipedema from lipohypertrophy or obesity? In 1996, Marshall used 18 kHz sonography to characterize the adipose tissue morphologically. He described a snow-flurries-like pattern without echo-less areas as characteristic for lipedema (Marshall, 1996). In a recent five-center trial, high resolution sonography provided no specific morphological findings to differentiate lipedema from other lipohypertrophic disorders (Hirsch, Schleinitz, Marshall, & Faerber, 2018).

Bariatric surgery is an invasive method to treat patients with morbid obesity. Even after successful bariatric surgery, lipedema has

**FIGURE 1** Clinical presentation of lipedema of the legs. (a) Stage 1 with positive cuff sign on the distal lower leg. (b) Stage 2 with telangiectasia. (c) Stage 3 with hemosiderosis and secondary lymphedema of the feet

been documented in patients not responding with the overall weight loss (Bast, Ahmed, & Engdahl, 2016; Wollina, Dreßler, & Lohmann, 2015).

5 | INFLAMMATION

We investigated whether tyrosine kinases might be involved in a postulated chronic low-level inflammation in adipose tissue of lipedema patients. Proteins from adipose tissue harvested during microcannular tumescent liposuction in lipedema were subjected to 10% polyacrylamide-gel, transferred to a polyvinylidene fluoride membrane and immunoblotted with indicated P-Tyr-100 antibody followed by enhanced chemiluminescence reaction. A survey of all blots did not reveal tyrosine-phosphorylated proteins with a molecular weight > 100 kD in lipedema tissue. These investigations suggest absence of activated growth factor receptors and exclude any enduring activation of tyrosine kinase pathways of adipogenesis in lipedema (Schneble, Wetzker, & Wollina, 2016).

6 | BRUISING

Lipedema-associated bruising has been considered as a consequence of an increased capillary fragility (CF). In a recent study CF was evaluated with the vacuum suction method using Parrot's angiosterrrometer (Arlotti & Serravalli, 1955). Application of vacuum suction resulted in a significantly higher number of petechiae in lipedema compared to obese patients (Szolnoky et al., 2017).

7 | PAIN

The pain in lipedema is a common complaint. Patients report spontaneous pain, pain on pressure and the feeling of tension, heaviness and burning (Wollina, 2017). White subcutaneous adipose tissue is innervated by sympathetic and sensory nerves. The adipocytes produce and release neurotrophic factors which are controlling the sensible innervation. The sensible nerves are primary unmyelinated C-fibers that are capable to forward pain sensations. The pain sensations in lipedema are unspecific. They can be regarded as a response to non-noceptive stimuli known as allodynia (Brenner, 2017).

8 | COMORBIDITIES

Comorbidities can be related to age, severity and duration of disease. The Dutch survey of Romeijn et al. (2018) observed comorbidities in 56.4%. The most frequent comorbidities were cardiac disease (21.5%), thyroid disease (11.7%), fibromyalgia (8.6%), and diabetes mellitus (5.5%) (Romeijn et al., 2018).

In a study involving 46 patients with lipedema there was a low risk of diabetes (2%), dyslipidemia (11.7%) and hypertension (13%) despite a median BMI of $35.3 \pm 1.7 \text{ kg/m}^2$ (Torre, Wadea, Rosas, & Herbst, 2018).

The lower risk of diabetes in lipedema patients nicely illustrates the different pathogenesis of lipedema and obesity. Central obesity is associated to diabetes mellitus (Riobó Serván, 2013).

9 | CONSERVATIVE TREATMENT

The complex decongestive therapy (CDT) has been the cornerstone of conservative treatment in lipedema patients implemented in several guidelines (Halk & Damstra, 2017; Reich-Schupke et al., 2017).

CDT depends upon manual lymph drainage, compression therapy using flat knitting compression garments and physical mobilization (Heinig & Wollina, 2015).

In a recent study, 30 patients with lipedema Stage 2 to 3 were treated in a two-armed approach with either six treatment with manual lymph drainage either alone or in combination with low frequency shock wave therapy. The extremity volume and the quality of life improved better with the combination (Schneider, 2018).

The usefulness of manual lymph drainage in lipedema has been questioned, as the edema is not an essential component of the disease (Bertsch & Erbacher, 2018b).

The Quadrivas Therapy[®], also known as subcutaneous adipose tissue therapy (SAT) is basically a massage therapy that is thought to activate microcirculation by intensive deep scraping and hook techniques. In the clinical trial NCT02907411, six patients with lipedema and one patient with Dercum's disease were treated by SAT with twelve 90-min sessions over 4 weeks. The body composition was evaluated by dual X-ray absorptiometry scan, leg volume, weight, pain, bioimpedance measurements, tissue size by caliper, and ultrasound before and after SAT therapy. The loss of weight (87.6 ± 21 to $86.1 \pm 20.5 \text{ kg}$), leg fat mass (17.8 ± 7.7 to $17.4 \pm 7.6 \text{ kg}$), and total leg volume (12.9 ± 4 to $12 \pm 3.5 \text{ L}$) reached significance in paired t test. However, pain scores remained unaffected (Ibarra et al., 2018).

10 | SURGICAL TREATMENT

Microcannular liposuction in tumescent anesthesia for lipedema has initially been described by Schmeller and Meier-Vollrath (2006). The method has become the gold standard of surgical treatment (Dadras, Mallinger, Corterier, Theodosiadi, & Ghods, 2017; Rapprich, Dingler, & Podda, 2011; Schmeller & Meier-Vollrath, 2006; Wollina, Goldman, & Heinig, 2010; Wollina & Heinig, 2012).

But does the method result in good long-term results? This has been a matter of debate. In a recent single-center study, 85 patients with lipedema were examined 4 years and 8 years after liposuction. The authors observed that compared with the results after 4 years, the improvement in spontaneous pain, sensitivity to pressure, edema, bruising and restriction of movement persisted. The same held true for patient self-assessment of cosmetic appearance, quality of life and overall impairment. Eight years after surgery, the reduction in the amount of conservative treatment (combined decongestive therapy, compression garments) was similar to that observed 4 years earlier (Baumgartner, Hueppe, & Schmeller, 2016).

In elderly patients with advanced lipedema, correction of increased skin laxity has to be considered for an optimal outcome. We combined tumescent microcannular laser-assisted liposuction of the legs and medial thigh lift and partial lower abdominoplasty with minimal undermining to correct skin laxity and prevent intertrigo. Postsurgical care with nonelastic flat knitted compression garments and manual lymph drainage are recommended (Wollina, Heinig, & Nowak, 2014).

As a rare complication of long-standing and advanced lipedema, elephantiasis nostras may develop. In two patients, debulking surgery with a modified Auchincloss-Kim technique was used successfully in addition to tumescent microcannular liposuction.

A vertical incision from the inner knee to just above the medial malleolus was made and raised anterior and posterior flaps, 1–2 cm thick, up to the midsagittal plane. This was followed by excision of the subcutaneous tissue down to the underlying deep fascia. The redundant skin was removed, and drains were placed. Skin and subcutaneous tissue was sutured in two layers. The leg was immobilized and elevated (Kim, Huh, Hwang, & Joh, 2004; Wollina, Heinig, Schönlebe, & Nowak, 2014).

Histologic data suggest that the ectatic lymphatic vessels of an immature phenotype. The findings explain the limitations of CDT and tumescent liposuction in such patients and their predisposition to relapsing erysipelas (Wollina, Heinig, Schönlebe, & Nowak, 2014).

11 | CONCLUSIONS AND OUTLOOK

Lipedema, often known as a forgotten disease, has gained more scientific and public interest in recent years. Lipedema can clearly be separated from lymphedema and obesity, although the diseases may all occur in a single patient. The most severe impairments result from pain and reduced physical mobility. These are the major targets of treatment, not edema. A better understanding of the interplay of pain, inflammation and disease progression is needed. Early diagnosis is warranted to avoid secondary complaints and comorbidities.

CONFLICT OF INTEREST

No conflicts of interest.

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REFERENCES

- Allen, E. V., & Hines, E. A., Jr. (1940). Lipedema of the legs: A syndrome characterized by fat legs and orthostatic edema. *Mayo Clinic Proceedings*, 15, 184–187.
- Arlotti, O., & Serravalli, S. (1955). Parrot's angiostrometer. *Progresso medico (Napoli)*, 11, 498–489.
- Bast, J. H., Ahmed, L., & Engdahl, R. (2016). Lipedema in patients after bariatric surgery. *Surgery for Obesity and Related Diseases*, 12, 1131–1132.
- Baumgartner, A., Hueppe, M., & Schmeller, W. (2016). Long-term benefit of liposuction in patients with lipoedema: A follow-up study after an average of 4 and 8 years. *British Journal of Dermatology*, 174, 1061–1067.
- Bertsch, T., & Erbacher, G. (2018a). Lipödem—Mythen und Fakten Teil 1. *Phlebologie*, 47, 84–92.
- Bertsch, T., & Erbacher, G. (2018b). Lipödem—Mythen und Fakten Teil 2. *Phlebologie*, 47, 120–126.
- Birkballe, S., Jensen, M. R., Noerregaard, S., Gottrup, F., & Karlsmark, T. (2014). Can tissue dielectric constant measurement aid in differentiating lymphoedema from lipoedema in women with swollen legs? *British Journal of Dermatology*, 170, 96–102.
- Brauer, W. J., & Weissleder, H. (2002). Methodik und Ergebnisse der Funktionslymphszintigraphie: Erfahrungen bei 924 Patienten. *Phlebologie*, 31, 118–125.
- Brenner, E. (2017). Wie kommt der Schmerz ins Lipödem? *Lymphologie in Forschung und Praxis*, 21, 45–47.
- Buck, D. W., 2nd, & Herbst, K. L. (2016). Lipedema: A relatively common disease with extremely common misconceptions. *Plastic and Reconstructive Surgery—Global Open*, 4, e1043.
- Dadras, M., Mallinger, P. J., Corterier, C. C., Theodosiadi, S., & Ghods, M. (2017). Liposuction in the treatment of lipedema: A longitudinal study. *Archives of Plastic Surgery*, 44, 324–331.
- Dietzel, R., Reissauer, A., Jahr, S., Calafiore, D., & Armbrrecht, G. (2015). Body composition in lipoedema of the legs using dual-energy X-ray absorptiometry: A case-control study. *British Journal of Dermatology*, 173, 594–596.
- Dudek, J. E., Białaszek, W., Ostaszewski, P., & Smidt, T. (2018). Depression and appearance-related distress in functioning with lipedema. *Psychology, Health & Medicine*, 23, 846–853.
- Fornier-Cordero, I., Oliván-Sasot, P., Ruiz-Llorca, C., & Muñoz-Langa, J. (2018). Lymphoscintigraphic findings in patients with lipedema. *Revista Española de Medicina Nuclear e Imagen Molecular*, pii: S2253-654X(18)30096-9, 37, 341–348. <https://doi.org/10.1016/j.remn.2018.06.008>
- Halk, A. B., & Damstra, R. J. (2017). First Dutch guidelines on lipedema using the international classification of functioning, disability and health. *Phlebologie*, 32, 152–159.
- Heinig, B., & Wollina, U. (2015). Komplexe Entstauungstherapie. *Der Hautarzt*, 66, 810–818.
- Herpertz, U. (2003). Der Mißbrauch des Lipödems. *Lymphologie in Forschung und Praxis*, 7, 90–93.
- Hirsch, T., Schleinitz, J., Marshall, M., & Faerber, G. (2018). Ist die Differenzialdiagnostik des Lipödems mittels hochauflösender Sonografie möglich? *Phlebologie*, 47, 182–187.
- Ibarra, M., Eekema, A., Ussery, C., Neuhardt, D., Garby, K., & Herbst, K. L. (2018). Subcutaneous adipose tissue therapy reduces fat by dual X-ray absorptiometry scan and improves tissue structure by ultrasound in women with lipoedema and Dercum disease. *Clinical Obesity*, 8, 398–406. <https://doi.org/10.1111/cob.12281>
- Kim, D. I., Huh, S. H., Hwang, J. H., & Joh, J. H. (2004). Excisional surgery for chronic advanced lymphedema. *Surgery Today*, 34, 134–137.
- Marshall, M. (1996). Differentialdiagnostische Abklärung des Lymph- und Phlebödems mittels hochauflösender (Duplex-)Sonographie. *Ultraschall in Klinik und Praxis*, 10, 130–137.
- Marshall, M., & Schwahn-Schreiber, C. (2011). Prävalenz des Lipödems bei berufstätigen Frauen in Deutschland (Lipödem-3-Studie). *Phlebologie*, 40, 127–134.
- Rappich, S., Dingler, A., & Podda, M. (2011). Liposuction is an effective treatment for lipedema—Results of a study with 25 patients. *Journal der Deutschen Dermatologischen Gesellschaft*, 9, 33–40.
- Reich-Schupke, S., Schmeller, W., Brauer, W. J., Cornely, M. E., Faerber, G., Ludwig, M., ... Ure, C. (2017). S1 guidelines: Lipedema. *Journal der Deutschen Dermatologischen Gesellschaft*, 15, 758–767.
- Riobó Serván, P. (2013). Obesity and diabetes. *Nutrición Hospitalaria*, 28 (Suppl. 5), 138–143.
- Romeijn, J. R. M., de Rooij, M. J. M., Janssen, L., & Martens, H. (2018). Exploration of patient characteristics and quality of life in patients with lipoedema using a survey. *Dermatologic Therapy (Heidelberg)*, 8, 303–311.
- Schmeller, W., & Meier-Vollrath, I. (2006). Tumescent liposuction: A new and successful therapy for lipedema. *Journal of Cutaneous Medicine & Surgery*, 10, 7–10.
- Schneble, N., Wetzker, R., & Wollina, U. (2016). Lipedema—Lack of evidence for the involvement of tyrosine kinases. *Journal of Biologic Regulators & Homeostasis Agents*, 30, 161–163.
- Schneider, R. (2018). Low-frequency vibrotherapy considerably improves the effectiveness of manual lymphatic drainage (MLD) in patients with lipedema: A two-armed, randomized, controlled pragmatic trial. *Physiotherapy*

- Theory and Practice*, 1–8. <https://doi.org/10.1080/09593985.2018.1479474>
- Shavit, E., Wollina, U., & Alavi, A. (2018). Lipoedema is not lymphoedema: A review of current literature. *International Wound Journal*, 15, 921–928.
- Stößenreuther, R. H. K. (2001). *Lipödem und Cellulitis sowie andere Erkrankungen des Fettgewebes*. Köln: Viavital.
- Szolnoky, G., Ifeoluwa, A., Tuczai, M., Varga, E., Varga, M., Dosa-Racz, E., & Kemeny, L. (2017). Measurement of capillary fragility: A useful tool to differentiate lipoedema from obesity? *Lymphology*, 50, 203–209.
- Torre, Y. S., Wadea, R., Rosas, V., & Herbst, K. L. (2018). Lipoedema: Friend and foe. *Hormone Molecular Biology and Clinical Investigation*, 33. <https://doi.org/10.1515/hmbci-2017-0076>
- Wollina, U. (2017). Das Lipödem: Aktuelle Aspekte einer lange vergessenen Erkrankung. *Wiener Medizinische Wochenschrift*, 167, 343–348.
- Wollina, U., Dreßler, M., & Lohmann, T. (2015). Bariatric surgery—A dermatologic perspective. *Journal of the European Academy of Dermatology & Venereology*, 29, 835–841.
- Wollina, U., Goldman, A., & Heinig, B. (2010). Microcannular tumescent liposuction in advanced lipoedema and Dercum's disease. *Giornale Italiano di Dermatologia e Venereologia*, 145, 151–159.
- Wollina, U., & Heinig, B. (2012). Tumescent microcannular (laser-assisted) liposuction in painful lipoedema. *European Journal of Aesthetic Medicine & Dermatology*, 2, 56–69.
- Wollina, U., & Heinig, B. (2018). Differenzialdiagnostik von Lipödem und Lymphödem. Ein Leitfaden für die Praxis. *Zeitschrift für Rheumatologie*, 77, 799–807. <https://doi.org/10.1007/s00393-018-0546-y>
- Wollina, U., Heinig, B., & Nowak, A. (2014). Treatment of elderly patients with advanced lipoedema: A combination of laser-assisted liposuction, medial thigh lift, and lower partial abdominoplasty. *Clinical, Cosmetic & Investigational Dermatology*, 7, 35–42.
- Wollina, U., Heinig, B., Schönlebe, J., & Nowak, A. (2014). Debulking surgery for elephantiasis nostras with large ectatic podoplanin-negative lymphatic vessels in patients with lipo-lymphedema. *Eplasty*, 14, e11.

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