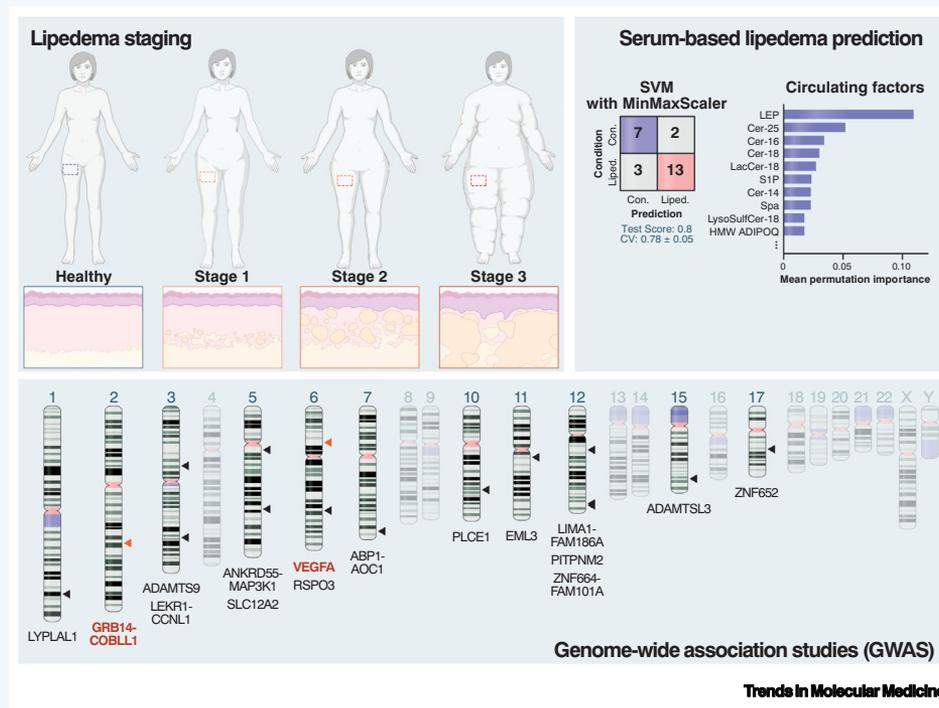


Lipedema: a chronic adipose tissue disease

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PREVALENCE:

- Initiatives for international consensus on disease classification are ongoing.
- Affects around 1–10% of women, depending on the diagnostic criteria used.
- Onset during puberty or pregnancy, with progression linked to hormonal shifts.

CLINICAL PHENOTYPES:

- Symmetrical accumulation of subcutaneous fat predominantly in the legs and at the hips.
- Reduced waist-to-hip ratio.
- Easy bruising, tenderness, and painfulness of affected areas.

DIAGNOSTICS:

- Lipedema (ICD-11, EF02.2) is a non-inflammatory disorder of subcutaneous fat.
- Visual inspection (symmetric fat in the legs, at the hips, and possibly arms in disproportion to trunk; lobules at the knees and ankles; cuffing and varicosities).
- Palpation (nodular, firm fat; painful, cold areas; negative Stemmer sign suggests lipedema; positive Stemmer sign suggests lipolymphedema or secondary lymphedema).
- Ultrasound and magnetic resonance imaging (MRI) (thickened, hypoechoic fat).
- Blood tests [elevated circulating vascular endothelial growth factor (VEGF), leptin, adiponectin, and ceramide levels]

COMORBIDITIES:

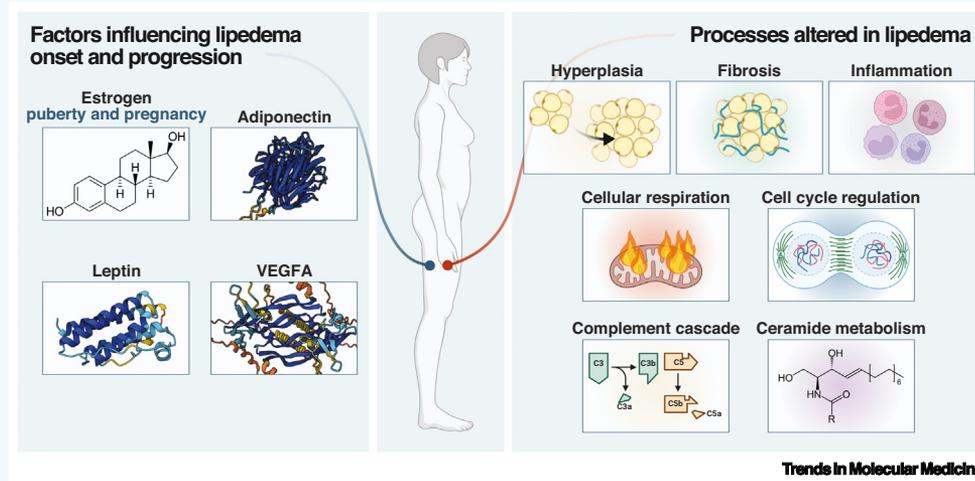
- Obesity
- Pain
- Chronic venous disease
- Lymphedema
- Anxiety and depression

TREATMENT:

- Compression therapy
- Dietary intervention
- Manual lymph drainage
- Low-impact exercise

Lipedema is a non-inflammatory disorder of subcutaneous fat mainly affecting women, manifesting as non-pitting, diffuse fat accumulation in legs, hips, and upper arms. It progresses through stages: stage 1 has even skin with small, rice-grain-sized fat nodules; stage 2 features uneven, larger fat nodules and fibrosis; stage 3 causes skin deformity from massive fat extrusions. Genome-wide association studies (GWAS) link polymorphisms in *VEGFA*, *GRB14-COBL1*, and other loci related to increased waist-to-hip ratio, and functionally connect vessel formation and lipid storage. A serum-based diagnostic test measuring adipokine and ceramide levels has been proposed.

Onset often occurs during puberty, pregnancy, or menopause, driven by hormonal shifts. Multiomics studies reveal increased cellular respiration and decreased leukocyte activation. Metabolic, vascular, and immune dysregulation – including aberrant local complement activity – may drive tissue remodeling and hyperplasia. The inability of adipocytes to integrate sex hormone signals as shown by dysregulation of adipokines, particularly at stage 1, is suggested to play a key role in disease development. Future research to investigate these mechanisms is urgently needed.



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BioRender.com was used in the creation of the figures.

Declaration of interests

The authors declare no competing interests.

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- Fat reduction through liposuction (can improve pain and mobility)
- No FDA-approved drugs available

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