

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/389426537>

Metabolic Therapy for Lipedema: Can Tirzepatide Overcome the Treatment Gap?

Article in *Journal of Pharmaceutical Research International* · February 2025

DOI: 10.9734/jpri/2025/v37i37664

CITATIONS

0

READS

2,448

2 authors:



[Diogo Pinto da Costa Viana](#)

SBEMEE

9 PUBLICATIONS 4 CITATIONS

[SEE PROFILE](#)



[Lucas Caseri Câmara](#)

53 PUBLICATIONS 220 CITATIONS

[SEE PROFILE](#)



Metabolic Therapy for Lipedema: Can Tirzepatide Overcome the Treatment Gap?

Diogo Pinto da Costa Viana ^{a*} and Lucas Caseri Câmara ^b

^a *Sociedade Brasileira de Endocrinologia e Metabologia do Esporte e Exercício, Brazil.*

^b *Department of Evidence Health Based Program, Federal University of São Paulo, Brazil.*

Authors' contributions

This work was carried out in collaboration between the two authors. Each author contributed substantially to the underlying research and approved the manuscript. Both authors read and approved the final manuscript.

Article Information

DOI: <https://doi.org/10.9734/jpri/2025/v37i37664>

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://pr.sdiarticle5.com/review-history/131897>

Opinion Article

Received: 19/02/2025

Accepted: 25/02/2025

Published: 28/02/2025

ABSTRACT

Aims: This article reviews the pathophysiological mechanisms of lipedema and explores the potential benefits of tirzepatide as a novel therapeutic approach.

Study Design: Opinion article.

Place and Duration of Study: Brazil, January–February 2025.

Methodology: A critical analysis of current literature on lipedema pathophysiology and tirzepatide's pharmacological effects, integrating evidence from metabolic, immunological, and fibrotic pathways.

Results: Lipedema is a chronic disorder of adipose tissue characterized by disproportionate fat accumulation, inflammation, and fibrosis, predominantly affecting women. Evidence suggests that an estrogen imbalance, rather than strict estrogen dependence, contributes to its pathophysiology.

*Corresponding author: E-mail: pinto.vianadiogo@gmail.com;

Despite its significant impact on quality of life, pharmacological treatment options remain limited, as lipedematous fat is resistant to caloric restriction, appetite-suppressing medications, and even bariatric surgery. Given recent advances in metabolic therapies, tirzepatide—a dual GLP-1 and GIP receptor agonist—has emerged as a promising candidate for lipedema management. Beyond its well-documented effects on weight loss and glycemic control, tirzepatide exhibits anti-inflammatory, antifibrotic, and thermogenic properties that target key mechanisms of lipedema. It modulates macrophage polarization, inhibits fibrosis-promoting pathways, and enhances energy expenditure via UCP1 activation in brown adipose tissue. However, despite its potential benefits, tirzepatide has yet to be formally evaluated for this condition.

Conclusion: This article critically appraises the rationale for tirzepatide as a therapeutic option for lipedema, discussing its potential benefits, limitations, and the urgent need for dedicated clinical trials to establish its efficacy and safety in this underserved patient population.

Keywords: *Lipedema; tirzepatide; anti-inflammatory agents; GLP-1; metabolic therapy.*

ABBREVIATIONS

Alfa estradiol receptors (ER α), Beta estradiol receptors (ER β), Dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1, 17 β -hydroxysteroid dehydrogenase (17 β -HSD), Tumor necrosis factor alpha (TNF- α), Interleucina-6 (IL-6), Mitochondrial uncoupling protein 1 (UCP1), A Study of Tirzepatide (LY3298176) in Participants With Obesity or Overweight (SURMOUNT-1), Glycated Haemoglobin (HbA1c), Glucagon-Like Peptide-1 (GLP-1), Preserved ejection fraction (HFpEF), Metabolic-associated steatohepatitis (MASH), Heart Failure With Preserved Ejection Fraction (HFpEF), M1 macrophage, M2 macrophages, Gastric inhibitory polypeptide (GIP), Monocyte chemoattractant protein-1 (MCP-1), extracellular regulated protein kinases (ERK)

1. INTRODUCTION

Lipedema is a chronic, progressive inflammatory disorder of adipose tissue that primarily affects women. The condition has a strong hormonal component, with evidence indicating an imbalance in estradiol receptor distribution in adipose tissue (ER α > ER β), contributing to adipocyte hypertrophy, inflammation, and fibrosis (Katzner et al., 2021). Epidemiological studies estimate a global prevalence ranging from 11% to 39% among adult women, depending on the diagnostic criteria used (Katzner et al., 2021; Buck & Herbst, 2016; Christoffersen & Tennfjord, 2023).

Unfortunately, lipedema is frequently underdiagnosed due to its symptomatic overlap with obesity and lymphedema. However, unlike these conditions, it is characterized by a disproportionate accumulation of subcutaneous fat in the upper and lower limbs, sparing the hands and feet. Its hormonal influence leads to

symmetrical and disproportionate fat deposition, accompanied by a pronounced inflammatory response that contributes to pain, fibrosis, and adipose tissue edema, distinguishing it from both obesity and lymphedema. One of the most challenging aspects of lipedema treatment—often a source of psychological distress, emotional disorders, and even eating disturbances among affected individuals—is its resistance to caloric deficit. Unlike obesity, lipedema does not respond to anorexigenic or satiety-inducing pharmacological strategies, nor to bariatric surgery (Allen & Hines, 1940; Wold et al., 1951).

Given that lipedema is a condition with both physical and psychological burdens that profoundly affect the well-being of many women (Clarke et al., 2023; Chachaj et al., 2024), with an estimated global prevalence of 10% (van la Parra et al., 2023), and that available therapeutic strategies remain insufficient, it is crucial to investigate alternative treatment options for these patients.

Due to the suboptimal efficacy of existing interventions, there is an urgent demand for innovative therapeutic solutions. Conservative measures provide only temporary symptom management without tackling the root cause of fat accumulation, while surgical techniques remain debated due to associated risks and the absence of standardized guidelines (Podda et al., 2021; Omaira et al., 2015). In this scenario, tirzepatide stands out as a potential breakthrough, with its dual GLP-1 and GIP receptor agonism offering a targeted approach to key pathophysiological aspects of lipedema, such as inflammation, fibrosis, and metabolic dysregulation.

Tirzepatide may represent a promising therapeutic option and a new hope for lipedema

management. Originally developed for the treatment of obesity associated with metabolic syndrome and diabetes (Rosenstock et al., 2021), its dual GLP-1 and GIP receptor agonism confers unique properties that could be particularly beneficial in lipedema treatment, including anti-inflammatory, antifibrotic, and thermogenic effects.

This article aims to review the pathophysiological mechanisms of lipedema, analyze the proposed mechanisms of action of tirzepatide, and explore its potential as a novel therapeutic approach for lipedema, particularly due to its well-established anti-inflammatory and metabolic effects.

2. PATHOPHYSIOLOGICAL MECHANISMS OF LIPEDEMA

Lipedema is a chronic, progressive condition influenced by genetic, hormonal, and environmental factors, with a particular emphasis on the imbalance between estradiol alpha (ER α) and beta (ER β) receptors in subcutaneous adipose tissue. This imbalance, present in all cases, predominantly affects the arms and legs in a disproportionate manner. Increased ER α expression promotes the expansion of dysfunctional adipose tissue, contributing to local inflammation, fibrosis, edema, and vascular and lymphatic dysfunction. Hormonal fluctuations during puberty, pregnancy, and menopause further exacerbate the disease, underscoring the critical role of estradiol in adipocyte dysfunction.

External factors, such as exposure to endocrine disruptors and xenoestrogens—primarily linked to unhealthy dietary patterns rich in processed foods, sugar, and other pro-inflammatory substances—further aggravate adipose tissue dysfunction (Annunziata et al., 2024). These disruptors interfere with estradiol metabolism, leading to increased ER α activation. Moreover, a strong correlation exists between lipedema and gynecological conditions, including endometriosis, fibroids, and progesterone resistance, which share common pathophysiological mechanisms such as elevated aromatase activity and dysregulation of key enzymes like 17 β -HSD. These alterations contribute to increased local estradiol levels (Seefeldt et al., 2023; Patton et al., 2024).

These findings underscore the necessity of integrated therapeutic approaches that address not only the metabolic and hormonal dimensions of the disease but also its gynecological implications (Viana & Câmara, 2025).

The increased activation of ER α ultimately drives the abnormal expansion of inflammatory adipose tissue, resulting in a pattern that is both symmetrical and disproportionate relative to other body regions. This process is primarily mediated by immunological alterations, microangiopathy, lymphatic dysfunction, and reduced thermogenesis (Szél et al., 2014; Felmerer et al., 2020a; Felmerer et al., 2020b; Poojari et al., 2022). Fig. 1 provides a comprehensive overview of lipedema, illustrating its morphology, pathophysiology, and the key challenges associated with the condition (Poojari et al., 2022).

From an immunological standpoint, the affected adipose tissue exhibits increased infiltration of pro-inflammatory M1 macrophages, contributing to a chronic inflammatory state marked by elevated levels of cytokines such as TNF- α and IL-6 (Felmerer et al., 2020a; Felmerer et al., 2020b).

Microangiopathy, a hallmark feature of lipedema, arises from endothelial dysfunction, increased vascular permeability, and hypoxia, collectively driving inflammation, fibrotic remodeling, and impaired nutrient delivery (Szél et al., 2014). These effects occur both mechanically, due to the compression of adjacent structures, and as a consequence of the inflammatory response.

Lymphatic dysfunction, characterized by micro-lymphatic aneurysms and morphological abnormalities displaying a "string-of-beads" pattern on MR lymphangiography, indicates both functional and structural impairment of lymphatic capillaries (Amann-Vesti et al., 2001). This dysfunction exacerbates interstitial fluid accumulation, which, in turn, perpetuates hypertrophic and fibrotic adipose tissue growth, establishing a self-sustaining cycle of tissue remodeling and lymphatic compromise (Poojari et al., 2022).

Additionally, reduced thermogenesis, linked to decreased expression of mitochondrial uncoupling protein 1 (UCP1) in affected tissues, limits energy expenditure and contributes to the metabolic inefficiency of lipedematous fat (Szél et al., 2014). Collectively, these mechanisms underscore the complexity of lipedema and the challenges associated with its therapeutic management, making the disease resistant to caloric deficit, anorexigenic pharmacological strategies, and even bariatric surgery (Pouwels et al., 2018; Cornely et al., 2022).

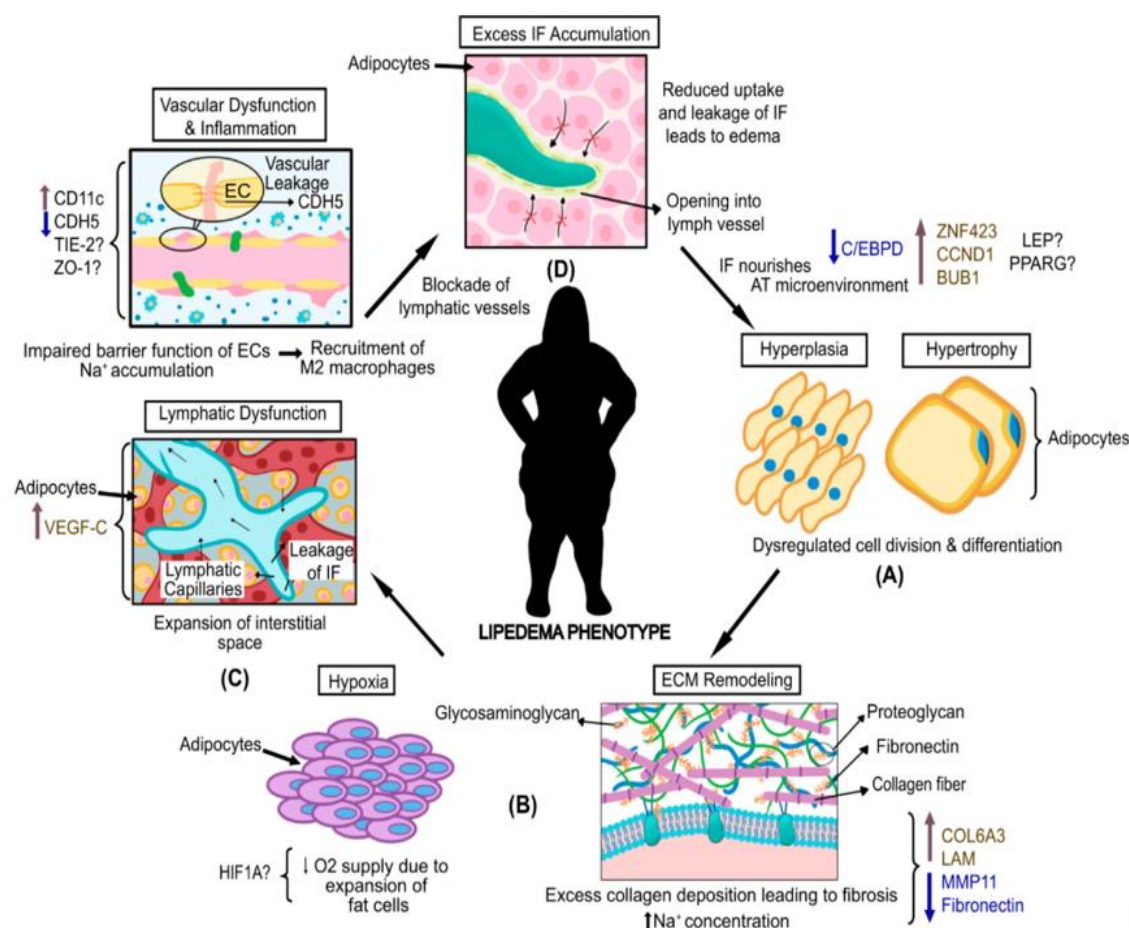


Fig. 1. Lipedema—insights into morphology, pathophysiology, and challenges

The sequence of events sustaining the lipedema phenotype follows this pattern: **(A)** Increased expression of genes associated with mitotic clonal expansion (MCE) and cell proliferation leads to adipocyte hyperplasia.

Although excessive lipid accumulation within adipocytes, resulting in hypertrophy, has been confirmed in lipedema, the expression of markers associated with this phenomenon remains a topic of debate. **(B)** Due to the excessive growth of adipocytes, oxygen supply is reduced, and extracellular matrix (ECM) remodeling is observed. This remodeling includes increased sodium (Na^+) concentration, collagen deposition, and disturbances in the glycocalyx (including proteoglycans and glycosaminoglycans), leading to microangiopathy and fibrosis. **(C)**

Endothelial permeability and paracellular leakage increase due to the weakening of tight junctions between endothelial cells (ECs), further exacerbating vascular impairment and inflammation. Additionally, the capacity of lymphatic capillaries to absorb interstitial fluid (IF) is reduced, promoting IF leakage, lymphatic dysfunction, and expansion of the interstitial space. **(D)** Pathogenic alterations at the vascular and lymphatic levels contribute to interstitial fluid accumulation, leading to fluid deposition. Excess IF surrounding adipocytes serves as a nutrient source, further driving pathological adipocyte expansion, ultimately leading to subcutaneous adipose tissue (SAT) remodeling and perpetuating the lipedema phenotype in a cyclical manner.

Color coding from the original text: **Blue:** Decreased gene expression in lipedema, **Brown:** Increased gene expression in lipedema e **Black:** Conflicting findings reported for these genes.

3. POTENTIAL EFFECTS OF TIRZEPATIDE ON LIPEDEMA

Tirzepatide was developed as a dual agonist of GLP-1 and GIP receptors, primarily designed to enhance glycemic control in patients with type 2 diabetes and to induce significant weight loss in individuals with obesity or overweight. Clinical trials, such as SURMOUNT-1, have demonstrated that tirzepatide, at doses of 15 mg,

10 mg, and 5 mg, resulted in average weight reductions of 20.9%, 19.5%, and 15%, respectively, surpassing semaglutide by up to 30% in weight-loss efficacy (Jastreboff et al., 2022).

Beyond its effects on body weight, tirzepatide has shown notable metabolic benefits, including reductions in fasting glucose, HbA1c, triglycerides, and visceral fat, as well as

improvements in insulin sensitivity—even in non-diabetic individuals (Xia et al., 2024; Varol et al., 2014). Its mechanism of action integrates GLP-1-mediated appetite suppression and decreased caloric intake with GIP-driven modulation of lipid metabolism and adipose tissue inflammation, thereby influencing body composition and metabolic control (Xia et al., 2024; Varol et al., 2014). These findings position tirzepatide as a promising therapeutic agent for obesity and related metabolic disorders.

Furthermore, tirzepatide has demonstrated significant benefits in conditions associated with fat accumulation and fibrosis, such as heart failure with preserved ejection fraction (HFpEF) and metabolic-associated steatohepatitis (MASH), due to its lipolytic, anti-inflammatory, and antifibrotic properties. In HFpEF, it reduces epicardial fat—an inflammatory reservoir linked to diastolic dysfunction—by promoting lipolysis and attenuating adipose tissue inflammation (Xia et al., 2024). Additionally, it modulates myocardial fibrosis by inhibiting the ERK pathway and decreasing pro-inflammatory cytokines such as TNF- α and IL-6, while improving insulin resistance and glycemic control, both critical factors in HFpEF pathogenesis (Liu et al., 2023; Wilson et al., 2022). In MASH, tirzepatide lowers hepatic fat content by enhancing insulin sensitivity and lipolysis, reprogramming hepatic macrophages toward an anti-inflammatory phenotype, and regulating genes involved in extracellular matrix remodeling, thereby reducing liver fibrosis (Xia et al., 2024; Varol et al., 2014). These mechanisms closely resemble those observed in lipedema, suggesting that tirzepatide may reduce fat accumulation, mitigate chronic inflammation, and decrease fibrosis, positioning itself as a promising yet unexplored therapeutic approach for this condition.

Polycystic ovarian syndrome (PCOS) is recognized as a metabolic-endocrine disorder strongly influenced by estrogen deficiency and insulin resistance. Studies have shown that the imbalance in GnRH pulsatility in PCOS is exacerbated by hyperinsulinemia and adipose tissue-derived inflammation, leading to androgen excess and impaired follicular maturation (Turki & Ammar, 2024). Due to the overlapping metabolic disturbances between PCOS and obesity—including leptin resistance, chronic low-grade inflammation, and adipose dysfunction—tirzepatide emerges as a promising therapeutic option. Through its dual action on GLP-1 and GIP receptors, the drug not only improves glucose metabolism but also modulates

adipokine signaling, potentially mitigating key drivers of PCOS pathophysiology (Jensterle et al., 2022). Like lipedema, PCOS is a condition regulated by the hormonal imbalance between estradiol and androgens.

By enhancing lipolysis through GIP receptor activation, tirzepatide may facilitate the mobilization of resistant fat—a hallmark of lipedema—thereby promoting volume reduction in affected areas (Xia et al., 2024). Simultaneously, its ability to suppress pro-inflammatory M1 macrophage activity while increasing anti-inflammatory M2 macrophages contributes to a less inflammatory tissue environment, potentially alleviating the pain and edema characteristic of the condition (Varol et al., 2014).

Additionally, by inhibiting ERK pathway signaling, tirzepatide decreases the production of inflammatory cytokines such as TNF- α , IL-6, and MCP-1, thereby interrupting the chronic inflammatory cycle characteristic of lipedema (Poojari et al., 2022; Xia et al., 2024). While its direct effects on extracellular matrix (ECM) component expression require further investigation, its ability to reduce biomarkers such as YKL-40—implicated in fibrosis and tissue remodeling in cardiovascular diseases (Wilson et al., 2022)—suggests a potential role in ECM regulation. These mechanisms, previously discussed, are well-established in the pathophysiology of lipedema.

Tirzepatide has been shown to influence brown adipose tissue by increasing the expression of thermogenesis-related genes, such as UCP-1, which enhances energy expenditure and reduces fat accumulation (Varol et al., 2014). In lipedema, this effect may contribute to improved thermogenesis by stimulating brown adipose tissue (BAT) metabolism, promoting the breakdown of branched-chain amino acids (BCAAs), and increasing intermediates of the tricarboxylic acid (TCA) cycle, including α -ketoglutarate, fumarate, and malate—suggesting greater mitochondrial uncoupling and metabolic activation (Samms et al., 2022). Furthermore, its ability to improve mitochondrial-lysosomal function (Liang et al., 2025) highlights a broader role in energy metabolism regulation and may support the conversion of white adipose tissue into brown, a key mechanism for counteracting the resistance of lipedematous tissue to fat loss.

These combined effects position tirzepatide as a groundbreaking therapeutic approach for

improving symptoms and quality of life in patients with lipedema. No other pharmacological intervention has demonstrated the ability to comprehensively target all key mechanisms underlying the disease. Even semaglutide, which may serve as an adjunct therapy in lipedema cases associated with obesity, lacks the capacity to address the fundamental drivers of inflammation and fibrosis (Cifarelli et al., 2025).

4. CONCLUSION

Tirzepatide emerges as a promising and innovative therapeutic approach for lipedema, integrating metabolic, anti-inflammatory, and antifibrotic effects that directly target the key pathophysiological mechanisms of the disease. Its ability to reduce resistant fat accumulation through enhanced lipolysis, shift macrophage profiles toward an anti-inflammatory M2 phenotype, and inhibit ERK pathway signaling contributes to decreased chronic inflammation and lower levels of cytokines such as TNF- α and IL-6. Additionally, tirzepatide mitigates fibrosis by modulating extracellular matrix remodeling, thereby improving adipose tissue elasticity (Varol et al., 2014).

Furthermore, tirzepatide enhances thermogenesis in brown adipose tissue by stimulating the expression of genes such as UCP-1, promoting increased energy expenditure and reducing fat accumulation (Xia et al., 2024). These effects surpass those of semaglutide, which, despite its efficacy in obesity management, does not sufficiently address the inflammation and fibrosis central to lipedema (Cifarelli et al., 2025).

However, dedicated clinical trials are necessary to confirm tirzepatide's efficacy and safety in lipedema patients, potentially opening new therapeutic avenues for a condition that has thus far lacked effective pharmacological treatments.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

The authors declare that generative AI was used solely during the final stage of manuscript preparation (post-writing) and exclusively for linguistic refinement in the English language (Name: ChatGPT; Version: GPT-4; Model: OpenAI's Large Language Model;

Source: OpenAI - <https://openai.com>). No original text was generated or substantively edited by the AI.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Allen, E., & Hines, E. (1940). Lipedema of the legs: A syndrome characterized by fat legs and orthostatic edema. *Proceedings of the Staff Meetings of the Mayo Clinic*, 15, 184–187.
- Amann-Vesti, B. R., Franzeck, U. K., & Bollinger, A. (2001, December). Microlymphatic aneurysms in patients with lipedema. *Lymphology*, 34(4), 170–175.
- Annunziata, G., Paoli, A., Manzi, V., Camajani, E., Laterza, F., Verde, L., Capó, X., et al. (2024, December). The role of physical exercise as a therapeutic tool to improve lipedema: A consensus statement from the Italian Society of Motor and Sports Sciences (Società Italiana di Scienze Motorie e Sportive, SISMeS) and the Italian Society of Phlebology (Società Italiana di Flebologia, SIF). *Current Obesity Reports*, 13(4), 667–679.
- Buck, D. W. 2nd, & Herbst, K. L. (2016, September 28). Lipedema: A relatively common disease with extremely common misconceptions. *Plastic and Reconstructive Surgery - Global Open*, 4(9), e1043.
- Chachaj, A., Jeziorek, M., Dudka, I., Sowicz, M., Adaszyńska, A., Truszyński, A., et al. (2024, December). Disability and emotional symptoms in women with lipedema: A comparison with overweight/obese women. *Advances in Clinical and Experimental Medicine*, 33(12), 1367–1377.
- Christoffersen, V., & Tennfjord, M. K. (2023, January 20). Younger women with lipedema, their experiences with healthcare providers, and the importance of social support and belonging: A qualitative study. *International Journal of Environmental Research and Public Health*, 20(3), 1925.
- Cifarelli, V., Smith, G. I., Gonzalez-Nieves, S., Samovski, D., Palacios, H. H., Yoshino, J., et al. (2025, March 1). Adipose tissue biology and effect of weight loss in women with lipedema. *Diabetes*, 74(3), 308–319.

- Clarke, C., Kirby, J. N., Smidt, T., & Best, T. (2023, January). Stages of lipoedema: Experiences of physical and mental health and health care. *Quality of Life Research*, 32(1), 127–137.
- Cornely, M. E., Hasenberg, T., Cornely, O. A., Ure, C., Hettenhausen, C., & Schmidt, J. (2022, May). Persistent lipedema pain in patients after bariatric surgery: A case series of 13 patients. *Surgical Obesity and Related Diseases*, 18(5), 628–633.
- Felmerer, G., Stylianaki, A., Hägerling, R., Wang, A., Ströbel, P., Hollmén, M., Lindenblatt, N., Gousopoulos, E. (2020, September). Adipose tissue hypertrophy, an aberrant biochemical profile and distinct gene expression in lipedema. *Journal of Surgical Research*, 253, 294–303.
- Felmerer, G., Stylianaki, A., Hollmén, M., Ströbel, P., Stepniowski, A., Wang, A., et al. (2020, July 2). Increased levels of VEGF-C and macrophage infiltration in lipedema patients without changes in lymphatic vascular morphology. *Scientific Reports*, 10(1), 10947.
- Jastreboff, A. M., Aronne, L. J., Ahmad, N. N., Wharton, S., Connery, L., Alves, B., et al. (2022, July 21). Tirzepatide once weekly for the treatment of obesity. *New England Journal of Medicine*, 387(3), 205–216.
- Jensterle, M., Herman, R., & Janež, A. (2022). Therapeutic potential of glucagon-like peptide-1 agonists in polycystic ovary syndrome: From current clinical evidence to future perspectives. *Biomedicines*, 10(8), 1989.
- Katzer, K., Hill, J. L., McIver, K. B., & Foster, M. T. (2021, October 29). Lipedema and the potential role of estrogen in excessive adipose tissue accumulation. *International Journal of Molecular Sciences*, 22(21), 11720.
- Liang, J., Liu, H., Lv, G., Chen, X., Yang, Z., Hu, K., et al. (2025). Exploring the molecular mechanisms of tirzepatide in alleviating metabolic dysfunction-associated fatty liver in mice through integration of metabolomics, lipidomics, and proteomics. *Lipids in Health and Disease*, 24(1), 8.
- Liu, Q., Zhu, J., Kong, B., Shuai, W., & Huang, H. (2023, July). Tirzepatide attenuates lipopolysaccharide-induced left ventricular remodeling and dysfunction by inhibiting the TLR4/NF-κB/NLRP3 pathway. *International Immunopharmacology*, 120, 110311.
- Omaira, M., Mehrotra, A., Fankhauser, M. J., Hrinczenko, B., & Dimitrov, N. V. (2015). Lipedema: A clinical challenge—revisited. *Journal of Advanced Medical and Medical Research*, 5(11), 1328–1337.
- Patton, L., Ricolfi, L., Bortolon, M., Gabriele, G., Zolesio, P., Cione, E., et al. (2024, January 27). Observational study on a large Italian population with lipedema: Biochemical and hormonal profile, anatomical and clinical evaluation, self-reported history. *International Journal of Molecular Sciences*, 25(3), 1599.
- Podda, M., Kovacs, M., Hellmich, M., Roth, R., Zarrouk, M., Kraus, D., et al. (2021). A randomised controlled multicentre investigator-blinded clinical trial comparing efficacy and safety of surgery versus complex physical decongestive therapy for lipedema (LIPLEG). *Trials*, 22, 758.
- Poojari, A., Dev, K., & Rabiee, A. (2022, November 30). Lipedema: Insights into morphology, pathophysiology, and challenges. *Biomedicines*, 10(12), 3081.
- Pouwels, S., Huisman, S., Smelt, H. J. M., Said, M., & Smulders, J. F. (2018, April). Lipoedema in patients after bariatric surgery: Report of two cases and review of literature. *Clinical Obesity*, 8(2), 147–150.
- Rosenstock, J., Wysham, C., Frías, J. P., Kaneko, S., Lee, C. J., Fernández Landó, L., et al. (2021, July 10). Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): A double-blind, randomised, phase 3 trial. *Lancet*, 398(10295), 143–155.
- Samms, R. J., Zhang, G., He, W., Ilkayeva, O., Droz, B. A., Bauer, S. M., et al. (2022). Tirzepatide induces a thermogenic-like amino acid signature in brown adipose tissue. *Molecular Metabolism*, 64, 101550.
- Seefeldt, T., Aitzetmüller-Klietz, M. L., Kückelhaus, M., Wiebringhaus, P., Hirsch, T., Harati, K., et al. (2023, June). Breaking the circle-effectiveness of liposuction in lipedema. *Journal of the German Society of Dermatology*, 21(6), 601–609.
- Szél, E., Kemény, L., Groma, G., & Szolnoky, G. (2014, November). Pathophysiological dilemmas of lipedema. *Medical Hypotheses*, 83(5), 599–606.
- Turki, T. G., & Ammar, J. W. (2024). Role of gonadotropin-releasing hormone, leptin hormone, luteinizing hormone, follicle-stimulating hormone, and obesity in polycystic ovarian syndrome. *International Journal of Scientific Research in Biological Sciences*, 11(4), 1–6.

- van la Parra, R. F. D., Deconinck, C., Pirson, G., Servaes, M., Fosseppez, P. (2023, September). Lipedema: What we don't know. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, 84, 302–312.
- Varol, C., Zvibel, I., Spektor, L., Mantelmacher, F. D., Vugman, M., Thurm, T., et al. (2014, October 15). Long-acting glucose-dependent insulinotropic polypeptide ameliorates obesity-induced adipose tissue inflammation. *Journal of Immunology*, 193(8), 4002–4009.
- Viana, D. P. D. C., & Câmara, L. C. (2025). Hormonal links between lipedema and gynecological disorders: Therapeutic roles of gestrinone and drospirenone. *Journal of Advanced Medical and Medical Research*, 37(2), 175–188.
- Wilson, J. M., Lin, Y., Luo, M. J., Considine, G., Cox, A. L., Bowsman, L. M., et al. (2022, January). The dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist tirzepatide improves cardiovascular risk biomarkers in patients with type 2 diabetes: A post hoc analysis. *Diabetes, Obesity and Metabolism*, 24(1), 148–153.
- Wold, L. E., Allen, E., & Hines, E. (1951). Lipedema of the legs: A syndrome characterized by fat legs and edema. *Annals of Internal Medicine*, 34(5), 1243–1250.
- Xia, Y., Jin, J., Sun, Y., Kong, X., Shen, Z., Yan, R., et al. (2024, December 25). Tirzepatide's role in targeting adipose tissue macrophages to reduce obesity-related inflammation and improve insulin resistance. *International Immunopharmacology*, 143(Pt 2), 113499.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of the publisher and/or the editor(s). This publisher and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© Copyright (2025): Author(s). The licensee is the journal publisher. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:

<https://pr.sdiarticle5.com/review-history/131897>