

## ALLEGATO MODULO 2.2 – Sezione C

**Nota per il compilatore:** *Tutti i campi sono obbligatori tranne quelli espressamente indicati come facoltativi.*

Sezione C - Fonti dell'evidenza scientifica e eventuali studi di valutazione economica	
1.c Indicare le evidenze cliniche ( <i>citare le fonti</i> )	<p>LINEE GUIDA</p> <p>Standard of care for lipedema in the United States  <a href="https://pubmed.ncbi.nlm.nih.gov/34049453/">https://pubmed.ncbi.nlm.nih.gov/34049453/</a></p> <p><b>GENETICA:</b></p> <ol style="list-style-type: none"> <li>1. Aldo-Keto Reductase 1C1 ( AKR1C1) as the First Mutated Gene in a Family with Nonsyndromic Primary Lipedema [Michelini et al. 2020]  <a href="https://pubmed.ncbi.nlm.nih.gov/32872468/">https://pubmed.ncbi.nlm.nih.gov/32872468/</a></li> <li>2. A Multi-Gene Panel to Identify Lipedema-Predisposing Genetic Variants by a Next-Generation Sequencing Strategy [Michelini et al. 2022]  <a href="https://pubmed.ncbi.nlm.nih.gov/35207755/">https://pubmed.ncbi.nlm.nih.gov/35207755/</a></li> <li>3. Genetics of lipedema: new perspectives on genetic research and molecular diagnoses. [Paolacci et al. 2019]  <a href="https://pubmed.ncbi.nlm.nih.gov/31298310/">https://pubmed.ncbi.nlm.nih.gov/31298310/</a></li> <li>4. Lipedema: an inherited condition [Child et al. 2010]  <a href="https://pubmed.ncbi.nlm.nih.gov/20358611/">https://pubmed.ncbi.nlm.nih.gov/20358611/</a></li> <li>5. Adipose Tissue Hypertrophy, An Aberrant Biochemical Profile and Distinct Gene Expression in Lipedema [Felmerer et al. 2020]  <a href="https://pubmed.ncbi.nlm.nih.gov/32407981/">https://pubmed.ncbi.nlm.nih.gov/32407981/</a></li> </ol> <p><b>FISIOPATOLOGIA, DIAGNOSI E TRATTAMENTO:</b></p> <ol style="list-style-type: none"> <li>1. Lipedema—Pathogenesis, Diagnosis, and Treatment Options [Kruppa et al. 2020]  <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7465366/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7465366/</a></li> <li>2. New Insights on Lipedema: The Enigmatic Disease of the Peripheral Fat [Bauer et al. 2019]</li> </ol>

<p><a href="https://pubmed.ncbi.nlm.nih.gov/31764671/">https://pubmed.ncbi.nlm.nih.gov/31764671/</a></p> <p>3. Lipedema: friend and foe [Herbst et al. 2018]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/29522416/">https://pubmed.ncbi.nlm.nih.gov/29522416/</a></p> <p>4. Lipedema: A Call to Action! [Buso et al. 2019]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/31544340/">https://pubmed.ncbi.nlm.nih.gov/31544340/</a></p> <p>5. Cause and management of lipedema-associated pain [Wollina et al 2021]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/33001552/">https://pubmed.ncbi.nlm.nih.gov/33001552/</a></p> <p>6. Update in the management of lipedema. [Forner-Cordero 2021]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/33870676/">https://pubmed.ncbi.nlm.nih.gov/33870676/</a></p> <p>7. Lipedema [Vyas et al. 2022]</p> <p><a href="https://www.ncbi.nlm.nih.gov/books/NBK573066/">https://www.ncbi.nlm.nih.gov/books/NBK573066/</a></p> <p><b>ISTOPATOLOGIA</b></p> <p>Key signaling networks are dysregulated in patients with the adipose tissue disorder, lipedema [Ishaq et al. 2022]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/34764426/">https://pubmed.ncbi.nlm.nih.gov/34764426/</a></p> <p>Adipose Stem Cells from Lipedema and Control Adipose Tissue Respond Differently to Adipogenic Stimulation In Vitro [Bauer et al. 2019]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/31461015/">https://pubmed.ncbi.nlm.nih.gov/31461015/</a></p> <p><b>IMPLICAZIONI ENDOCRINE E VASCOLARI</b></p> <p>Lipedema and the Potential Role of Estrogen in Excessive Adipose Tissue Accumulation [Katzner et al. 2021]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/34769153/">https://pubmed.ncbi.nlm.nih.gov/34769153/</a></p> <p>Dilated Blood and Lymphatic Microvessels, Angiogenesis, Increased Macrophages, and Adipocyte Hypertrophy in Lipedema Thigh Skin and Fat Tissue [Al-Ghadban et al 2019]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/30949365/">https://pubmed.ncbi.nlm.nih.gov/30949365/</a></p> <p>The MMP14-caveolin axis and its potential relevance for lipoedema [Kruglikov et al. 2020]</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/32792644/">https://pubmed.ncbi.nlm.nih.gov/32792644/</a></p> <p><b>LIPEDEMA MALATTIA RARA</b></p> <p>Rare adipose disorders (RADs) masquerading as obesity [Herbst 2012]</p>
---

<https://pubmed.ncbi.nlm.nih.gov/22301856/>

Lipedema, a rare disease [Wook Shin et al. 2011]

<https://pubmed.ncbi.nlm.nih.gov/22506222/>

#### **DIAGNOSTICA STRUMENTALE**

1. Ultrasound criteria for lipedema diagnosis  
<https://pubmed.ncbi.nlm.nih.gov/33853452/>
2. Non-contrast MR Lymphography of lipedema of the lower extremities [Cellina et al. 2020]  
<https://pubmed.ncbi.nlm.nih.gov/32561380/>
3. Lymphoscintigraphic findings in patients with lipedema [Forner-Cordero 2018]  
<https://pubmed.ncbi.nlm.nih.gov/30166264/>
4. Characterizing Lower Extremity Lymphedema and Lipedema with Cutaneous Ultrasonography and an Objective Computer-Assisted Measurement of Dermal Echogenicity [Iker et al. 2019]  
<https://pubmed.ncbi.nlm.nih.gov/30615553/>

#### **CHIRURGIA DEL LIPEDEMA (LIPEDEMA REDUCTION SURGERY)**

1. Liposuction for the Treatment of Lipedema: A Review of Clinical Effectiveness and Guidelines [Peprah et al. 2019]  
<https://pubmed.ncbi.nlm.nih.gov/31479212/>
2. Prevention of Progression of Lipedema With Liposuction Using Tumescent Local Anesthesia: Results of an International Consensus Conference [Sandhofer et al. 2020]  
<https://pubmed.ncbi.nlm.nih.gov/31356433/>
3. Liposuction in the Treatment of Lipedema: A Longitudinal Study [Dadras et al. 2017]  
<https://pubmed.ncbi.nlm.nih.gov/28728329/>

	<ol style="list-style-type: none"><li>4. High Volume Liposuction in Tumescence Anesthesia in Lipedema Patients: A Retrospective Analysis [Sandhofer et al. 2021] <a href="https://pubmed.ncbi.nlm.nih.gov/33683073/">https://pubmed.ncbi.nlm.nih.gov/33683073/</a></li><li>5. Water-jet-assisted liposuction for the treatment of lipedema: Standardized treatment protocol and results of 63 patients [Witte et al. 2020] <a href="https://pubmed.ncbi.nlm.nih.gov/32446570/">https://pubmed.ncbi.nlm.nih.gov/32446570/</a></li><li>6. Management of large volume liposuction in lipedema patients with von Willebrand disease: A systematic review and treatment algorithm [Schmidt et al. 2021] <a href="https://pubmed.ncbi.nlm.nih.gov/33814418/">https://pubmed.ncbi.nlm.nih.gov/33814418/</a></li><li>7. Surgical treatment of Lipoedema [Ghods et al. 2018] <a href="https://pubmed.ncbi.nlm.nih.gov/30620978/">https://pubmed.ncbi.nlm.nih.gov/30620978/</a></li><li>8. Treatment of lipedema by low-volume micro-cannular liposuction in tumescent anesthesia: Results in 111 patients [Wollina et al 2019] <a href="https://pubmed.ncbi.nlm.nih.gov/30638291/">https://pubmed.ncbi.nlm.nih.gov/30638291/</a></li></ol> <p><b>NUTRIZIONE e DIAGNOSI DIFFERENZIALE</b></p> <ol style="list-style-type: none"><li>1. Ketogenic diet as a potential intervention for lipedema [Keith et al. 2021] <a href="https://pubmed.ncbi.nlm.nih.gov/33303304/">https://pubmed.ncbi.nlm.nih.gov/33303304/</a></li><li>2. Persistent lipedema pain in patients after bariatric surgery: a case series of 13 patients [Cornely et al. 2022] <a href="https://pubmed.ncbi.nlm.nih.gov/35144895/">https://pubmed.ncbi.nlm.nih.gov/35144895/</a></li><li>3. Lipoedema is not lymphoedema: A review of current literature [Shavit et al. 2018] <a href="https://pubmed.ncbi.nlm.nih.gov/29956468/">https://pubmed.ncbi.nlm.nih.gov/29956468/</a></li></ol> <p><b>FISIOTERAPIA E RIABILITAZIONE</b></p> <ol style="list-style-type: none"><li>1. The Effects of Complete Decongestive Therapy or Intermittent Pneumatic Compression Therapy or Exercise Only in the Treatment of Severe Lipedema: A Randomized Controlled Trial [Atan et al. 2021] <a href="https://pubmed.ncbi.nlm.nih.gov/33297826/">https://pubmed.ncbi.nlm.nih.gov/33297826/</a></li><li>2. Physiotherapy and rehabilitation applications in lipedema management: A literature review [Esmer et al. 2020] <a href="https://pubmed.ncbi.nlm.nih.gov/33190432/">https://pubmed.ncbi.nlm.nih.gov/33190432/</a></li></ol>
--	---

	<p>3. Physical Therapy in Women with Early Stage Lipedema: Potential Impact of Multimodal Manual Therapy, Compression, Exercise, and Education Interventions [Donahue et al. 2021]  <a href="https://pubmed.ncbi.nlm.nih.gov/34748408/">https://pubmed.ncbi.nlm.nih.gov/34748408/</a></p> <p>4. Reducing Circumference and Volume in Upper Extremity Lipedema: The Role of Complex Decongestive Physiotherapy [Volkan-Yazici et al. 2022]  <a href="https://pubmed.ncbi.nlm.nih.gov/33798399/">https://pubmed.ncbi.nlm.nih.gov/33798399/</a></p> <p>5. Pilot study: whole body manual subcutaneous adipose tissue (SAT) therapy improved pain and SAT structure in women with lipedema [Herbst et al. 2017]  <a href="https://pubmed.ncbi.nlm.nih.gov/28930626/">https://pubmed.ncbi.nlm.nih.gov/28930626/</a></p> <p><b>MENTAL HEALTH E QUALITY OF LIFE</b></p> <p>1. The effect of lipedema on health-related quality of life and psychological status: a narrative review of the literature [Alwardat et al 2020]  <a href="https://pubmed.ncbi.nlm.nih.gov/31062201/">https://pubmed.ncbi.nlm.nih.gov/31062201/</a></p> <p>2. Depression and appearance-related distress in functioning with lipedema [Dudek et al. 2018]  <a href="https://pubmed.ncbi.nlm.nih.gov/29614880/">https://pubmed.ncbi.nlm.nih.gov/29614880/</a></p>
<p>2.c Quali sono gli outcomes principali?</p>	<p>Con il trattamento chirurgico si attende un incremento della qualità di vita in 84% dei pazienti e una riduzione del dolore nel 86% dei pazienti.</p> <p>Si veda in proposito:</p> <p>Survey Outcomes of Lipedema Reduction Surgery in the United States [Herbst et al. 2021]  <a href="https://pubmed.ncbi.nlm.nih.gov/33912372/">https://pubmed.ncbi.nlm.nih.gov/33912372/</a></p> <p>Improvements in patients with lipedema 4, 8 and 12 years after liposuction [Baumgartner et al. 2021]  <a href="https://pubmed.ncbi.nlm.nih.gov/32847472/">https://pubmed.ncbi.nlm.nih.gov/32847472/</a></p> <p>A 10-Year Retrospective before-and-after Study of Lipedema Surgery: Patient-Reported Lipedema-Associated Symptom Improvement after Multistage Liposuction [Kruppa et al. 2022]  <a href="https://pubmed.ncbi.nlm.nih.gov/35089257/">https://pubmed.ncbi.nlm.nih.gov/35089257/</a></p>

3.c Citare eventuali studi di valutazione economica: Analisi Costo-Efficacia (CEA-COST-EFFECTIVENESS ANALYSIS) o Analisi Costo Utilità (CUA-COST-UTILITY ANALYSIS) o Analisi Costi Benefici (CBA-COST-Benefit ANALYSIS) <i>(facoltativo)</i>	Non sono pubblicati a data odierna.