# Diagnostic scales and methods for assessing the severity of gynoid lipodystophy

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### Abstract

**Objective:** The aim of this article is to collect and compare lipodystrophy assessment and severity grading methods. Electronic databases, bibliographies, and specialist publications were reviewed.

Methods: Medical databases and repositories of scientific articles were reviewed, including PubMed, Scopus, PMC-NCBI, Science.gov, and Google Scholar. Specialized publication sources were also searched. Based on the collected material, a list of available cellulite assessment and severity grading methods was prepared.

**Results:** The article presents all available scales for examining the advancement of cellulite changes. Based on available data and scales, it is possible to estimate the actual severity of GLD. Due to the multifactorial pathogenesis of the changes, the selection of appropriate treatment and prevention methods depends on good diagnostics. Conclusions: The conducted literature research allowed us to select papers published in the selected databases concerning comparative lipodystrophy assessment and severity grading methods. The obtained material will facilitate the selection of proper therapy and contribute to appropriate diagnostics, prevention, and treatment of changes. It will also facilitate understanding the pathophysiology and genesis of GLD.

### Introduction

Gynoidal lipodystrophy (GLD), oedema-fibrous-degenerative paniculopathy, most frequently called "cellulite" is a severe symptom of incorrect functioning of an organism which causes changes to subcutaneous adipose tissue and dermal compartment, changing the look of the skin.<sup>[1]</sup> It presents mainly in women between 80 and 98 percent in characteristic locations such as: thighs, hips, knees, buttocks, arms in the form of nodules and thickening of the surface of the skin, sometimes causing pain.<sup>[2]</sup> Throughout life, a woman's body undergoes various physiological changes. These changes may cause inflammatory relationships that may contribute to the occurrence of various types of diseases, such as: tissue ischemia, physiological imbalances, e.g. glycemic problems, stress, obesity, hormonal imbalances (puberty, pregnancy), menopause, menstrual cycle and body aging.<sup>[3]</sup> However, in healthy men, cellulite is rare, but may be observed as a result of diseases causing androgen deficiency or prostate cancer requiring estrogen treatment.<sup>[4]</sup>

The occurrence of GLD in women is related to morphological, biochemical and structural changes. The process of appearance of changes in the course of cellulite develops in subcutaneous adipose tissue and dermal compartment in stages, which may last for multiple months and even years.<sup>[5]</sup> Despite clear differences in the anatomy between the skin and the subcutaneous tissue and dermal compartment they are both structurally and functionally connected by a network of vessels and nerves and the presence of epidermis appendages.<sup>[6]</sup> The structure of the subcutaneous tissue is divided into vertical compartments, the structure of which resembles a honeycomb evenly spaced in the tissue, perpendicular to the more superficial layers of the skin.<sup>[7]</sup> Subcutaneous tissue is formed by adipose lobules interleaved with clearly defined fibrous tracts (reticula cutis superficialis), formed from elastin and collagen fibres placed perpendicularly to the skin surface. The adipose lobules are strongly anchored in the dermis, which connects them with the superficial fascia of the skin. They are located between the dermis and the superficial fascia of the skin and provide a transition to the vessels and nerves from the subcutaneous tissue.<sup>[8]</sup> Due to the anatomy of the subcutaneous tissue the GLD concerns women. The adipose lobules in women are larger and have parallel partitions. Whereas in men, the partitions of adipose lobules are smaller and placed in oblique planes with small pieces of fat.<sup>[9]</sup> In magnetic resonance imaging (MRI) examinations have observed the presence of papillae in the dermis only in women.<sup>[10]</sup>

Differences exist in the cellular structure of women and men, in different placement of estrogen receptors in endothelium cells, and also in capillaries of muscle cells, which causes differences in micro-circulation. The role of intercellular transport regulator for substances which have an impact on circulation, vasoconstrictive, fibrinolitic and antithrombotic is provided by endothelium.<sup>[11]</sup>

The aetiology of cellulite is multi-factorial. The patophysiology of occurrence of oedema-fibrous-degenerative changes is complex. This mechanism includes the proliferation of subcutaneous adipose tissue, the formation of fibrous partitions in the dermis, flaccidity and at-

rophy of the skin.<sup>[12]</sup> Predisposing factors for the development of cellulite include hormonal changes, genetic factors, familial inclination to incorrect deposition of adipose tissue, and insufficiently developed muscle mass.<sup>[1]</sup> During the first stage of development of gynoidal lipodystrophy changes to connective tissue, microcirculation disorders and stagnation within blood and lymphatic vessels occur, which as a consequence result in increased permeability of the vessels.<sup>[5]</sup> Insufficient regulation of intercellular transport of substances results in the decrease of vein tension and their expansion, which deteriorates drainage, results in water retention in the body and in oedemas. The increase of the amount of water compresses the adipose tissue, and the adipose cells receive less nutrition.<sup>[13]</sup> These processes impact the incorrect structure of adipocytes, which are entwined by spreading collagen fibres. The adipocytes are weakly oxygenated due to oxidative stress. This results in the creation of deformed and degenerated adipocytes, which become fibrous and then form nodules in the tissue, penetrating deep into the dermis, resulting in a characteristic "mattress-like" irregularities of the skin.<sup>[14]</sup> The characteristic for women's anatomy hernias in the dermis were confirmed by high-resolution magnetic resonance examination in the low-density areas of the dermis.<sup>[9]</sup> Cellulite is a dystrophic process with complex patophysiology with multiple interconnected factors which have an impact through various mechanisms (described above) in the connective and subcutaneous tissue. The disease has a genetic factor, and the hormone estrogen is its trigger, which in combination with other endogenous and exogenous factors starts a slow, progressive cascading reaction.<sup>[8]</sup> Already in 1920, skin changes resembling "orange peel" were noticed.[15] Today, cellulite is not only an aesthetic problem, but also a pathological condition, a disease which may contribute to or intensify other disorders and changes within the subcutaneous tissue, such as distended blood vessels, micro-varicose veins, oedemas, thickening and nodules appear, which may cause pain. Changes may be also observed in the form of loss of elasticity and flexibility, and in the form of skin flac-cidity.<sup>[5, 16]</sup>

Diagnosing is based on: anamnesis and physical examination, and diagnostics with the use of specialised equipment. When performing an anamnesis, data are collected on the history of diseases, such as: obesity, diabetes , chronic venous insufficiency of the lower limbs in parents, the age of first menstruation, hormonal disorders, number of pregnancies and deliveries, age of the first symptoms of menopause and the use of hormone replacement therapy as well as oral contraceptives.<sup>[17,18]</sup> There are important questions about the patient's history of weight, rapid weight gain or loss. In the case of mothers, it is very important to know by how many kilograms their body weight increased before childbirth in relation to their weight before pregnancy. Eating habits, fluid intake and physical activity are also of great importance.<sup>[19]</sup> After an anamnesis is conducted, a physical examination is performed, which consists of looking at the examined area of the body and palpating the changes, both at rest and in muscle tension. The skin appearance parameters, its wrinkling, colour, warmth, texture, the presence of telangiectasias, micro-varicose veins and stretch marks are taken into account. Special equipment or appropriate methods are also used during diagnostic examinations. The assessment involves the use of an anthropometric method, which measures body weight, height, muscle mass and fat mass, and also calculates the body mass index. The thickness of subcutaneous tissue, the degree of obesity and the distribution of adipose tissue are all assessed. However, this method does not accurately assess the degree of cellulite severity.<sup>[20]</sup> In examining the lipodystrophy severity, it is necessary to use appropriate measurement scales. The classification of cellulite distinguishes four degrees of cellulite development related to clinical, thermographic and histopathological changes, which are presented on individual measurement scales.<sup>[21]</sup>

The aim of this article is to collect and compare lipodystrophy assessment and severity grading methods.

## **Materials and Methods**

Medical databases and repositories of scientific articles were reviewed. PubMed, Scopus, PMC-NCBI, Science. gov, Google Scholar databases were used. Specialised publication sources were also searched. The keywords in building database queries were: lipodystrophy, gynoid lipodystrophy, gynoid lipodystophy cellulite, gynoid lipodystrophy therapy, gynoid lipodystrophy etiology, cellulite, gynoid cellulite, physiology of cellulite, anatomy of cellulite, cellulite pathophysiology, adipose cellulite, cellulite diagnostics, lipodystrophy measurement scales, lipodystrophy assessment methods, cellulite measurement scales, cellulite assessment methods. On this basis, a scientific databases search procedure was developed. Electronic databases were searched using Boolean operators.

The search concept is presented in Table 1.

	Table 1. Search strategy			
Database	Search Strings	Search Period	Obtained Articles	Articles Meeting Inclusion Criteria
Pub Med	gynoid: «gynoid»[All Fields] OR «gynoidal"[All Fields]			
	lipodystrophy: «lipodystrophy»[MeSH Terms] OR "lipodystrophy"[All Fields] OR "lipodystrophies"	2012-2022	6	3
	[All Fields] gynoid: «gynoid»[All Fields] OR «gynoidal"[All Fields]		[Appendix A]	
	cellulite: «cellulite»[MeSH Terms] OR "cellulite"[All Fields] OR "cellulites"[All Fields]			
PMC-NCBI				
	((cellulite) OR lipodystrophy) AND gynoid AND («open access»[filter] AND «last 10 years»[PDat] AND ( "nih funded" [Filter] OR "ahrq funded"[Filter] ) )	2012-2022	4	2
			[Appendix B]	
	(( TITLE-ABS-KEY ( lipodystrophy )OR TITLE-ABS-KEY ( cellulite ) AND TITLE-ABS-KEY ( gynoid ) )			
	gynoid)) AND (LIMIT-TO(PUBSTAGE, "final")) AND (LIMIT-TO(OA, "all")) AND (LIMIT-		12	5
	TO (PUBYEAR, 2022) OR LIMIT-	2013-2022	[Appendix C]	
	TO (PUBYEAR, 2021) OR LIMIT-			
	TO (PUBYEAR, 2020) OR LIMIT-			
	TO (PUBYEAR, 2019) OR LIMIT-			
Scopus	TO (PUBYEAR, 2018) OR LIMIT-			
	TO (PUBYEAR, 2017) OR LIMIT-			
	TO (PUBYEAR, 2016) OR LIMIT-			
	TO (PUBYEAR, 2015) OR LIMIT-			
	TO (PUBYEAR, 2014) OR LIMIT-			
	TO (PUBYEAR, 2013) AND (LIMIT-TO (DOCTYPE, «ar") OR LIMIT- TO (DOCTYPE, "re") OR LIMIT-TO (DOCTYPE, "ch") OR LIM- IT-TO (DOCTYPE, "cp"))			
Google Scholar				
	Lipodystrophy OR cellulite AND gynoide time limit	2012-2022	14	4
			[Appendix D]	
Scence.gov	Lipodystrophy OR cellulite AND gynoide AND women	2012-2022	13	5
			[Appendix E]	
Total		1978-2022	140	42
		1770 2022	[Appendix F]	12

#### Inclusion criteria

The inclusion and eligibility criteria for the analysis included: adults, female sex. The search included full and review publications, published in the period from 2012 to 2022. Articles in Polish, English and Spanish were qualified. Due to their special scientific value, materials from 1978, 1987, 2002, 2004, 2005 and 2010 were included.

#### **Exclusion criteria**

Exclusion criteria included: editorials, minutes, conference summaries; only free repositories of full-text publications were used.

The literature selection process began with an analysis of the titles. The search resulted in 473 publications. It was noticed that some of the publications received were duplicated and therefore duplicates were removed. As a result, 140 items remained. Subsequently, the abstracts were assessed and 78 articles were qualified for the final, full review in the next stage.

As a result, the list of publications in Appendix F was obtained.

Full articles were checked for relevance. The material was classified by consensus (M. B., P. S., S.A.), which resulted in 42 references.



Figure 1. Scheme for conducting a literature review

Grey literature was also included in the review, and 2 items were obtained. During the assessment of credibility of grey literature, the author's name and the presence of other publications by the same author were taken into account. Sources of the publication and the publisher were also assessed. The confirmation of the facts was checked in other sources. The analysis demonstrated that the majority of the literature on the assessment of cellulite includes items from 1978 (Nürnberger and Müller) and 2000 (Rossi). In the included review, 20 titles contained the 'cellulite' descriptor and 5 titles contained the 'review' descriptor. From the collected literature, 8 titles contained the 'treatment' expression.

### **Results:**

Based on the literature review, the following measurement scales were distinguished:

- 1. Nürnberger-Müller scale;
- 2. Anatomical and histopathological scale;
- 3. Histopathological scale;
- 4. Clinical and histopathological scale;
- 5. Clinical, thermographic and histopathological scale;

The classification of lipodystrophy changes by degree of advancement is a simple matter. Various methods of diagnosing these changes have been described in the literature. The best known and most widely used division is the classification according to Nürnberger and Müller. In 1978, they were the first to propose a palpation measurement scale related to clinical changes. The scale is based on the degrees of severity of changes, from 0 to 3. They conducted the first studies on human cadavers, with the goal of establishing anatomical causes of adipose tissue disorders. After the conducted examinations, they have arrived to partially incorrect conclusions. The authors have established that skin dimples and irregularities are characteristic to women, not to cellulite. They have also established that cellulite may not be classified, and that it is a characteristic feature of female anatomy, and not a disease.<sup>[22]</sup> They investigated the influence of changes in the cross-section of subcutaneous tissue on the occurrence of cellulite in relation to sex. They noticed differences in the structure of subcutaneous tissue between women and men. This differentiation already occurs in the fetal life of a child and is related to the influence of androgens on the activity of fibroblasts.<sup>[4]</sup> The authors described the formation of hernias of adipose tissue penetrating the dermis, which is characteristic for female anatomy. The dermis partitions in women are much thinner and distributed radially, compared to women without cellulite, thus facilitating extrusion of adipose tissue into the reticular layer of the dermis. Changes in the structure of subcutaneous tissue are located radially and perpendicularly to the skin surface, creating rectangular chambers in the surface layer separated by partitions - 'fat lobules' (papillae adiposae), which are protruding into the dermis and the reticulate layer. On the other hand, in men, these

partitions are arranged diagonally, creating smaller and polygonal chambers.<sup>[23]</sup> Due to their anatomical structure, women are predisposed to an irregular and discontinuous border between the dermis and subcutaneous tissue, characterised by the presence of adipose tissue reaching the dermis. On the other hand, the border between the dermis and adipose tissue and connective tissue in men is smooth and continuous. Women have a much greater number of adipocytes, characterised additionally by large size and ability to store larger amounts of lipids.<sup>[24]</sup> A literature review has not found articles which state that changes may not be classified. What's more, in subsequent years researchers have attempted to find scales that would facilitate the classification of changes and to introduce them in diagnostics. The method of classification proposed by the authors, even though it is not ideal, is still used today in beauty salons, in physiotherapy clinics and medical clinics in order to diagnose lipodystrophic changes.<sup>[25]</sup>

Table 2 Visual and palpation scale (Nürnberger and Müller) <sup>[12, 22]</sup>				
Stage of cellulite	Description of the stage			
0	Healthy skin, no dimpling when pressing the skin			
1	Smooth skin in both standing and lying positions			
2	Dimpling of the skin visible only in the standing position; in the lying position the skin is smooth			
3	Dimpling of the skin visible both in the standing and lying positions			

In 2010, changes in the structure of the skin with cellulite were noticed by Tomaszkiewicz and colleagues. They developed a four-level scale which, apart from visual changes, also took into account anatomical and histopathological changes.<sup>[26]</sup>

Table 3 Anatomical and histopathological scale		
Stage of cellulite	Description of the stage	
1	No clear visual changes in the skin, changes in the subcuta- neous tissue structure, pathological changes in microcircu- lation, the surface of the skin is evenly warmed	
2	Muscle contraction or tissue compression, which cause local ischaemia and paling, uneven warming of the skin surface (areas with reduced temperature appear), noticeable reduction in skin elasticity, more pronounced disorders in the adipose tissue structure	
3	Depressions of the skin ('mattress' effect) are noticeable in the resting position, lumpy thickenings in subcutaneous tissue are noticeable, pain appears as a result of a small squeeze, clear disturbances in the temperature distribution of the skin surface (numerous areas of low temperature), adipose tissue fibrosis	
4	Visible changes in the skin surface, as in the case of the 3 <sup>rd</sup> degree changes, but much more intense, adipose tissue fibrosis and inflammation, visible changes in microcirculation.	

In 2000, Rossi and colleagues described a histopathological method of examining lipodystrophic changes.<sup>[27]</sup> They proved that the effect of estrogens is one of the main factors causing cellulite changes, because their action dilates blood vessels and increases the permeability of their walls. Fluid escaping from the vessels starts accumulating in intercellular spaces, as a result of which lymphoedema presses on adipocytes. Adipocyte metabolism is thus disturbed and fat cells proliferate.

The lipoprotein lipase enzyme is affected by estrogens. The estrogens influence the stimulation of uptake and transport of free fatty acids to the inside of the cell, as well as the activity of chylomicron and VLDL (very-low-density lipoprotein) hydrolysis and the release of components necessary for HDL (high-density lipoprotein) synthesis. The lipoprotein lipase is an enzyme which is related to the endothelium in adipose tissue and in the muscles. This enzyme is regulated by hormonal activity. The action of lipoprotein lipase enzyme is stimulated by insulin and glucocorticoids, while the inhibition of the lipoprotein lipase enzyme is provided by catecholamines, growth hormone and testosterone. Additionally, increasing the volume of adipocytes has an influence on the increase of the lipoprotein lipase enzyme's activity, which increases lipogenesis. The increase of lipogenesis releases further growth of adipocytes. The lipolysis process results in formation of lumps and nodules and in fibrosis and hardening, thus resulting in the symptom of cellulite.<sup>[28]</sup>

Lipolysis and lipogenesis are processes that are opposite to each other. They both impact the metabolism of fat present in the human body (mainly in the subcutaneous tissue). When they operate correctly, the homeostasis of the organisms is not perturbed. Biological processes occurring inside the body self-regulate. However, if there exists a continuous excess in the supply of food, or when food is consumed in an irregular pattern, the activity of fat metabolism becomes disrupted and a growth of fat tissue occurs.<sup>[22, 29]</sup> The increase of lipogenesis induces the growth of adipocytes, causing a change in their shape and size. The process of lipogenesis, fibrosis and hardening of the partitions contributes to the formation of lumps and nodules, with cellulite as a symptom.<sup>[30]</sup>

Table 4 Histopathological scale     [27]		
Stage of cellulite	Description of the stage	
1	Tissue oedema, breakdown and changes in the structure of adipocytes, dilation and thickening of the endothelium of venous and arterial vessels	
2	Adipocyte degeneration symptoms , hyperplasia and hyper- trophy of reticulate and silverophilic fibres, cutaneous and subcutaneous microangiopathy, microhaemorrhages	
3	Collagenosis and apparent reduction in the number of ad- ipocytes, micronodules, blurring of the boundary between the skin and subcutaneous tissue, dysmorphism of papillae adiposae, local hyperkeratosis and liposclerosis	
4	Disappearance of the typical lobular structure, larger nodules, diffuse liposclerosis, large microvascular chang- es, atrophic-dystrophic changes of the epidermis and skin appendages, blurring of the boundary between the skin and subcutaneous tissue	

In 2011, Zegarska and colleagues described a relationship between the occurrence of cellulite and age, sex and body composition. Based on the literature on the subject, they took into account clinical and histopathological changes in the course of cellulite.<sup>[31]</sup> They described adipose tissue changes with age, sex and body composition. They performed microscopic observations which demonstrated that the appearance of the skin in the course of cellulite is influenced by degenerative changes in subcutaneous tissue of an oedematous-fibrotic-degenerative nature. This material was obtained using scanning microscopy methods to conduct detailed examination of subcutaneous tissue, collecting of a fragment of tissue from the areas afflicted with cellulite, and using a system for digital recording of images.

Table 5 Clinical and histopathological scale     [31]				
Stage of cellulite	Description of the stage			
1	No clinical changes are visible on the surface of the patient's skin (visible during a microscopic examination). There are changes in adipose tissue vessels, and venous and lymphatic stasis occurs. The reticulate layer thickens, the permeability of the capillaries increases, the capillaries dilate, and micro- haemorrhages and spindle-shaped microaneurysms appear in the post-capillary venous vessels. Adipocytes increase in size and form small clusters. Intracellular oedema occurs, leading to gradual damage to collagen and elastin fibres, and then to their breakdown.			
2	Symptoms are visible 'with the naked eye' and there is pain while pressed. There is a visible hypertrophy and hyper- plasia of silverophilic fibres around the capillaries and fat cells. Capillaries dilate, microhaemorrhages appear and the thickness of the capillary basement membrane increases.			
3	Symptoms visible 'with the naked eye', and when applying pressure pain is felt. The changes have a distinct 'orange peel' or 'mattress' appearance at rest. There is a signifi- cant decrease in elasticity, the skin pales and decreases in temperature. There is a visible thinning of adipose tissue. It is a result of formation of new collagen fibres, followed by encapsulation of small clusters of deformed adipocytes, which in turn causes the formation of micronodules and microlumps. Hardening and thickening of the lining of the inner layer of arterioles, dilation of venules, and the forma- tion of microaneurysms and haemorrhages within adipose tissue occur. New capillaries are formed and the border between the skin and subcutaneous tissue is blurred. The micronodules increase in volume and change their shape, fat cells harden and penetrate into the connective tissue of the deep layers of the dermis. Deposits of fibres and the ba- sic substance of connective tissue build up around the accu- mulated fat lobules, which leads to fibrosis of subcutaneous tissue, and circulatory disturbances are also intensified.			
4	All the stage 3 symptoms are present, and collagen deposits are transformed into hard nodules that press on the capil- laries and nerve fibres, causing soreness. The nodules are more palpable, visible and painful, and the skin surface becomes wrinkled. The changes are also visible at rest, even after muscles have relaxed. A histological examination revealed a disappearance of the lobular structure of adipose tissue, and adipose lobules are surrounded by highly fibrotic connective tissue, forming numerous nodules. The microscopic image also shows diffuse liposclerosis, which precedes microcirculation disturbances. There are telangi- ectasias, micro-varicose veins and varicose veins as well as epidermal atrophy.			

In 2014, Janda and Tomikowska, based on the literature on the subject, described clinical, thermographic and histopathological changes in the skin and subcutaneous tissue.<sup>[16]</sup> They explored the causes, prevention and treatment of cellulite. They described factors influencing the appearance of lipodystrophy, hormonal disorders, excess estrogen with simultaneous progesterone deficiency. The phenomena of adipocyte hyperplasia and water accumulation, circulatory disturbances were observed. An increase in pressure in the capillaries causes an increase in the permeability of venous vessels, and slows down blood flow, as a result of which oedema occurs. Insulin, catecholamine

(adrenaline and noradrenaline) and thyroid hormones also play an important role in the course of cellulite. The lipoprotein lipase mechanism used by female organism to store fat in the body is responsible for the formation of cellulite. The impact of circulation regulating, vasoconstrictive, fibrinolytic and anti-inflammatory substances on the deposition of adipose tissue is regulated by the lipoprotein lipase enzyme, which is connected with the endothelium.<sup>[11]</sup> Adipose tissue is present in women in characteristic locations such as: thighs, hips, abdomen, buttocks. These locations are at an increased risk of the presence of cellulite.<sup>[5]</sup> Differences in the areas of metabolic and hormonal activity of the adipose tissue are also a factor influencing the occurrence of gynoidal lipodystrophy.<sup>[1]</sup> The catecholamine stimulated lipolytic activity is higher within the visceral fat tissue than within the abdominal subcutaneous tissue, and is the lowest within the gluteal and thigh tissue area. The increased response to mixed adrenergic receptor agonists, such as epinephrine and norepinephrine, of the abdominal adipose cells, as opposed to the adipose cells in the gluteal area is the reason for the formation of cellulite in this area.<sup>[32,33]</sup> An incorrect diet with excessive consumption of fats and carbohydrates, is also important, causing hyperinsulinemia and intensification of lipogenesis.<sup>[29]</sup>

Table 6 Clinical, thermographical and histopathological scale		
Stage of cellulite	Description of the stage	
	Clinical changes: reduced skin elasticity,	
1	Thermographic changes: foci of hyperaemia clearly sur- rounded by areas of ischaemia,	
-	Histopathological changes: tissue oedema, breakdown and changes in the structure of adipocytes, dilatation and thick- ening of the endothelium of venous and arterial vessels;	
	Clinical changes: reduced skin elasticity, pale skin, 'negative pinch test',	
2	Thermographic changes: foci of hyperaemia not clearly demarcated from areas of ischaemia,	
	Histopathological changes: degenerative symptoms of adipocytes, hyperplasia and hypertrophy of reticulate and silverophilic fibres, cutaneous and subcutaneous microangi- opathy, microhaemorrhages;	
	Clinical changes: reduced skin elasticity, pale skin, 'pinch test' locally positive, presence of small lumps, 'orange peel',	
	Thermographic changes: large foci of ischaemia, 'leopard skin',	
3	Histopathological changes: collagenosis and an apparent reduction in the number of adipocytes, micronodules, blurring of the border between the skin and subcutaneous tissue, dysmorphism of papillae adiposae, local hyperkerato- sis and liposclerosis;	
	Clinical changes: reduced skin elasticity, pale skin, positive 'pinch test', formation of larger lumps,	
4	Thermographic changes: large foci of ischaemia, the 'leopard skin' and the 'black hole' area,	
Ť	Histopathological changes: disappearance of the typical lobular structure, larger nodules, diffuse liposclerosis, large microvascular changes, atrophic-dystrophic changes of the epidermis and skin appendages, blurring of the boundary between the skin and subcutaneous tissue.	

The diagnostics of cellulite, degree of advancement and clinical assessment of the changes are not easy. The authors adopt many criteria, and choosing one of the scales is not an easy task. The classification of cellulite and clinical changes taking place in subcutaneous tissue can also be made by observation of the consistency of the skin by performing a palpation examination and a 'pinch test', i.e., Godet test of lipodystrophic changes.<sup>[34]</sup> When performing a palpation examination, one can feel the layers of the skin, the boundaries between the skin and subcutaneous tissue, and the presence of lumps in the formation of cellulite, which are noticeable after folding the skin. When performing a thermographic examination, lipodystrophic changes in the form of hyperaemia or ischaemia of tissues that are separated from healthy areas are noticeable.<sup>[35]</sup> The diagnosis of lipodystrophic changes is most often based on a visual and palpation examination and the use of the scale proposed in 1978 by Nürnberger and Müller. Other authors proposed the use of measurement scales based on clinical, thermographic or histopathological examination.<sup>[36]</sup>

In addition to the palpation and visual methods, anthropometric methods as well as the BMI (Body Mass Index) and WHR (Waist Hip Ratio) measures are used.<sup>[26]</sup>

The articles did not deal with methods of archiving of data obtained during the examination of lipodystrophic changes.

As indicated by studies, electronic record keeping improves the decision-making process, decreasing the amount of work required. Maintaining the documentation on an ongoing basis and storing it on electronic media enables comparison of the undertaken cosmetology interventions. The availability and reliability of electronic devices is as important. One of many electronic systems is "ADPIE-Care Dorothea", used for the ordering of interventions and for provision of compherensive nursing care.<sup>[37]</sup>

### Discussion

Based on the lipodystrophic changes listed in the tables above, it can be observed that the diagnostics of cellulite and the unambiguous assessment of the degree of advancement of the changes is not easy. The authors adopt many criteria and choosing one of the scales is not an easy task. The diagnostics of lipodystrophic changes can be divided into diagnosistics of clinical, thermographic and histopathological changes.<sup>[16, 31, 38]</sup> Clinical changes occurring in subcutaneous tissue can be examined by palpating lipodystrophic changes, observing skin consistency.<sup>[39]</sup> Classification of thermographic changes can be made by performing an examination with a thermal imaging camera.<sup>[40, 41]</sup> The pathogenesis of the changes is multifactorial, and determining the exact degree of advancement of the changes is a challenge for modern medicine. In order to choose the right therapy, and implement appropriate methods of treatment, it is necessary to correctly diagnose the type of cellulite. It is extremely important to correctly select diagnostic tools that would enable a quick diagnosis of the degree of advancement of the changes and an objective assessment of treatment progress.

Classic visual and palpation examination methods provide less objective assessment of the skin surface affected by cellulite, compared with non-contact thermography. The visual assessment of lipodystrophic changes is not very precise and neither very objective nor accurate. The physical examination consists of looking at the examined area of the body and palpating the changes, both at rest and in muscle tension. The examination is burdened with many errors, such as: the influence of the presence of telangiectasias, micro-varicose veins and stretch marks on the appearance of cellulite-covered skin.

Venous changes cause disturbances in microcirculation, which may cause a misdiagnosis in combination with visible telangiectasias or varicose veins. Measurement errors may also result from the variable characteristics of lipodystrophy. People with lipodystrophic changes, may have different degrees and varieties of cellulite, depending on the location of the changes. The visual and palpation examination, despite the fact that it was introduced in 1978 by Nürnberger and Müller and is burdened with such a high risk of measurement error, is still used today to assess cellulite.<sup>[22]</sup> That is why it is so important to find an appropriate and precise method of assessing lipodystrophic changes. Based on the theory that cellulite is characterised by disrupted circulation, the imaging techniques of laser Doppler flowmetry and videocapillaroscopic thermography are more detailed than the visual and palpation examination of lipodystrophic changes.<sup>[42]</sup> Ultrasonography of the skin and subcutaneous tissue is a method which enables the detection of lipodsystrophic nodules, assessment of their diameter and of connective tissue structure.<sup>[43]</sup> The Doppler examination shows the measurement of skin microcirculation, the image of arterial and venous activity, which make the diagnosis accurate, and the detected symptoms of venous insufficiency and images of lipodystrophic changes can be saved in a computer program.<sup>[44]</sup> The computer thermography examination also enables an accurate assessment of lipodystrophy, by measuring and recording the heat of the skin with cellulite. Lipodystrophic changes show a different warmth than healthy skin. This enables the creation of histograms, which allow for an accurate assessment of the severity of the changes. The use of this method enables early detection of lipodystrophic and venous changes, determining the exact degree of their severity and monitoring the progress of treatment.<sup>[40]</sup> The use of appropriate, repeatable multiple methods of examination of cellulite changes enables the objective inspection of the degree of intensity of changes and effective use of an appropriate method of lipodystrophy therapy.

Proper diagnosis of lipodystrophic changes is a very important aspect in the selection of a therapy, in order to ensure the chosen method of treating the changes is the most effective and long-lasting. The problem of health is based not only on the correct diagnostics of the changes, but also on the mental and aesthetic comfort of the patients.<sup>[45]</sup> Lipodystrophic changes negatively affect the self-esteem and well-being of women, significantly diminishing their quality of life. The more advanced the cellulite is, the greater the psychological discomfort of women. The disease also has a negative impact on the patient's health.<sup>[46]</sup>

### Conclusion

The conducted literature research allowed us to select papers which were published in selected databases concerning comparative lipodystrophy assessment and severity grading methods. Afterwards, the contents of the selected articles were analysed. Knowledge of all the scales will enable an accurate assessment of the severity of the changes, and will facilitate the selection of one of the scales, which will contribute to the correct diagnosis and further treatment. The objectivity of results of paniculopathy severity assessment is problematic due to the variability in the occurrence of the changes in the patients. Increasing the understanding of complexity of cellulite pathology and a correct diagnosis of the severity of the changes will improve the possibility of targeted treatment and of further developments in the field of diagnostics in the near future. The clinical picture of lipodystrophy is diverse and, depending on the stage of the disease, a diagnosis of the changes is difficult. The changes are not only of an aesthetic nature, in the appearance of the skin, but most of all they are lesions that carry the risk of impaired microcirculation in connective tissue, as a result of which telangiectasias and micro-varicose veins may occur.

It is important to find a combination of all available measurement scales or to develop one reliable scale in order to be able to properly diagnose the observed severity of lipodystrophic changes. Currently, there are multiple measurement scales that all have flaws, are not objective and do not provide meaningful results. Therefore, from this point of view, it is necessary to develop a new scale, that will enable an objective and repeatable assessment of the advancement of lipodystrophic changes.

# 6. Supplementary Data

Appendix A PUB MED PMC data 20.03.2022

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Appendix C Scopuus Search Results 20.03.- 4.04.2022

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