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Date of prep: May 2023 | UK/OTHR/NP/21/0043

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Body mass index vs. waist-to-height-ratio in patients with lipohyperplasia dolorosa (vulgo lipedema)

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Summary

Background: Lipedema, also known as lipohyperplasia dolorosa (LiDo), is a painful condition affecting women, causing a disproportionate accumulation of subcutaneous adipose tissue in the extremities. It carries a lower risk of diabetes and cardio-metabolic dysfunctions compared to obesity, but coincident obesity can complicate diagnosis and treatment.

Patients and Methods: This retrospective study included 607 female LiDo patients, ≥ 18 years, stage 1–3, from Germany, the UK, and Spain. Data were collected as part of the standard initial assessment for LiDo patients.

Results: Based on waist-to-height-ratio (WHtR), 15.2% of patients were underweight, 45.5% normal weight, 22.1% overweight and 17.3% obese. There was a significant association between WHtR category and age group. Body mass index (BMI) is often overestimated, leading to misdiagnosis of obesity.

Conclusions: The use of BMI also affects the recent decision of the German Federal Joint Committee on the reimbursement of liposuction costs by health insurance funds. Patients with BMI of more than 40 kg/m^2 are excluded from cost coverage, and those with BMI between 35 kg/m^2 and 40 kg/m^2 must first receive conservative obesity therapy. In conclusion, the sole use of BMI in lipedema is unreliable and, in contrast to WHtR, leads to inaccurate diagnoses overestimating overweight and obesity.

KEYWORDS

Lipedema, body mass index, waist-to-height ratio, coincident obesity

INTRODUCTION

Lipedema (ICD-11: EF02.2; ICD-10, German Modification Version 2022: E88.20–E88.22) is a painful, disproportionate accumulation of subcutaneous adipose tissue (SAT) in the lower and, less commonly, upper limbs, almost exclusively in women. The trunk and head are not affected, nor are the feet or hands. To distinguish between the painful condition “lipedema” and the painless condition “lipohypertrophy”¹, Cornely proposed the term “lipohyperplasia dolorosa” (LiDo).²

While the sparse earlier publications cited low incidence and prevalence, in recent years the number of new diagnoses appears to have exploded.^{3,4}

In contrast to obesity, the exclusive accumulation of SAT in LiDo has been associated with a lower risk for diabetes and other cardio-metabolic dysfunctions.^{5–7} Insulin resistance is less pronounced in LiDo patients with obesity than in patients with obesity but without LiDo, despite a higher average weight. This difference disappears with increasing abdominal obesity.⁸

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There are no known circulating biomarkers that could facilitate the diagnosis of LiDo.⁷

On September 19, 2019, the Federal Joint Committee (G-BA) of Germany decided that the health insurance funds would cover the costs of surgical liposuction in patients with LiDo stage 3 under certain conditions.⁹ The Federal Joint Committee is the highest decision-making body of the joint self-government of physicians, dentists, hospitals and health insurance funds in Germany. Coincident obesity (body mass index, BMI, ≥ 35 kg/m² and < 40 kg/m²) must be treated in an appropriate manner before liposuction is indicated. LiDo patients with a BMI > 40 kg/m² are excluded from liposuction. The changes have been effective since January 2020 and are valid until December 2024. Approved hospitals and contract physicians perform surgical liposuction both as outpatient and inpatient procedures. This decision of the G-BA is related to a trial study started in 2018, investigating the effectiveness of conservative therapy and liposuction in LiDo patients stages 1–3, primarily concerning pain.^{10,11}

Coincident overweight or obesity complicates the diagnosis and, thus, the therapy of LiDo. The respective extent of the contribution of these two conditions to a patient's appearance may be difficult to determine. LiDo is, by definition, confined to the extremities, excluding the feet or hands, and always painful.^{12,13} However, being overweight or obese can also dramatically increase SAT in the extremities.

In both the diagnosis of LiDo^{12–14} and research on this disease, the BMI is used to assess the metabolic situation of patients. The fundamental problem is that the BMI increases with the disproportionate increase of SAT of the extremities in LiDo, even in metabolically normal, i.e., “normal weight” patients. This makes a valid classification of the metabolic risks – and therefore coincident obesity – impossible. It is not possible to see whether the weight gain is due only to LiDo or to LiDo and coincident obesity. Therefore, the BMI lacks construct validity.

Research designs that classify the metabolic risks of the study group by BMI or that adjust the control group according to BMI could therefore probably be comparing participants with very different metabolic situations.

A better alternative is the relation between waist circumference and height (waist-to-height-ratio, WHtR). The WHtR is unaffected by total weight and, thus, by the weight of the legs or arms and exclusively reflects the nutritional condition. Apparently, Wold et al.¹⁵ have already determined the WHtR of 50 of their 119 female patients, but without giving further details; only mean height (160 cm) and mean body weight (68 kg) are reported.

A study of 5,956 women from Germany provides a solid population for categorization.¹⁶ For these authors, WHtR is an ideal candidate and a simple tool for assessing obesity-associated risks. They defined a cut-off level of 0.5 for women aged up to 40 years and 0.6 for women aged 50 years or older to give a reasonable assessment of the future risk of death and cardiovascular events. For the age group

TABLE 1 Categorization of health risks according to WHtR.^{16,17}

Age [years]	< 15	15–40	41–50	> 50
Obesity Grade II	> 0.63	> 0.68	+ 0.01/year	> 0.78
Obesity Grade I	0.52–0.63	0.57–0.68	+ 0.01/year	0.67–0.78
Overweight	0.46–0.51	0.51–0.56	+ 0.01/year	0.61–0.66
Normal weight	0.34–0.45	0.40–0.50	+ 0.01/year	0.50–0.60
Underweight	< 0.34	< 0.40	+ 0.01/year	< 0.50

between 40 and 50 years, the cut-off levels should lie somewhere between 0.5 and 0.6. Based on these data, it was proposed to increase the cut-off level by 0.01 per year in this age-group.¹⁷

The waist-to-height-ratio has clear advantages. While BMI includes all fat (also the “healthy” fat in the extremities) and even muscle mass, WHtR primarily considers abdominal fat, which is crucial for assessing health risks. Table 1 summarizes the categories according to WHtR.

There are only a few LiDo studies that at least mention WHtR, although they do not use it for the classification of metabolic risks.^{18–22} Our study aims to determine the distribution of WHtR in LiDo patients and to compare it with their BMI. The primary question is what WHtR patients with reliably diagnosed LiDo and any coincident overweight or obesity present. The secondary question aims to determine how these LiDo patients match a general population. Therefore, we compared our data with the previously mentioned study of 5,956 German women.¹⁶

PATIENTS AND METHODS

For this analysis of anthropometric measurements, data of 466 female LiDo patients' records over 18 years of age from four centers in Germany and Spain were collected retrospectively. The data were part of the standard initial assessment for LiDo patients (Table 2). Diagnosis and morphological staging were made clinically using standard criteria.^{12,13} Patients with stage 4 (lipo-lymphedema), and previous surgical treatment for LiDo were excluded. Additionally, patients with an apparent asymmetry of the two lower extremities or side difference over 5% were excluded.

Additionally, we included data from 132 patients from the “UK Lipoedema cohort”,²³ published supplementally. We included data of those patients whose weight, height, and waist measures were available. Data from patients who reported having had previous liposuction were excluded.

From these data, we calculated BMI (Formula 1) and WHtR (Formula 2).

Formula 1: Body Mass Index

$$BMI \left[\text{kg/m}^2 \right] = \frac{\text{Body Weight} \left[\text{kg} \right]}{\text{Body Height}^2 \left[\text{m}^2 \right]}$$

TABLE 2 Data collected for each patient.

ID	Consecutive number per center
Source	Short name of the center
Age [years]	Age of the patient at assessment
Diagnosis	usually, LiDo
Stage	Stage of LiDo
Weight [kg]	Body weight in kilograms
Height [cm]	Body height in centimeters
Waist measure [cm]	Waist circumference in centimeters
Hip measure [cm]	Hip circumference in centimeters
cG _{right} [cm]	Stocking measurement: circumference at the height of point G on the right thigh in centimeters; optional
cG _{left} [cm]	Stocking measurement: circumference at the height of point G on the left thigh in centimeters; optional
Volume _{right} [cm ³]	Volume of the right leg in cubic centimeters, optional
Volume _{left} [cm ³]	Volume of the left leg in cubic centimeters, optional

Formula 2: Waist-to-Height-Ratio

$$WHtR = \frac{\text{Waist Circumference [cm]}}{\text{Body Height [cm]}}$$

The BMI was categorized according to the WHO classification,²⁴ and WHtR according Schneider et al. and Stemper (Table 1).^{16,17}

Descriptive statistics were obtained for all variables. For continuous variables, mean, standard deviation (SD) and median are presented, and absolute and relative frequencies were obtained for categorical variables. Finally, categorical variables were compared using the chi-square test and continuous variables with the analysis of variance (ANOVA).

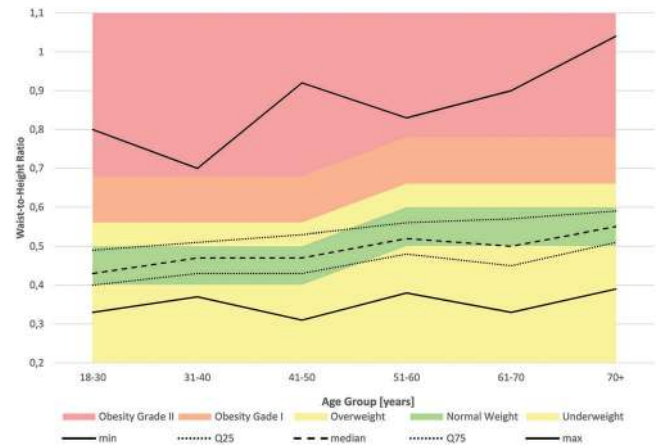
For statistical analysis, we used PSPP (GNU pspp 1.6.2-g78a33a; Free Software Foundation Inc.).

Ethics

The study was approved by the Ethics Committee of the Medical University of Innsbruck (EC No. 1196/2022) and registered by the Clinical Trial Center (20220930-3004; <https://ctc.tirol-kliniken.at/page.cfm?vpath=oeffentliche&action=viewdetail&studie=17942>).

RESULTS

Figure 1 superimposes the categories¹⁷ with the quartile data of the WHtR of 5,956 German women.¹⁶ Women within the interquartile range (Q₂₅: Q₇₅) are normal-weight in most cases, whereas women in the first quartile are under-

**FIGURE 1** Quartile data by Schneider et al. (2010),¹⁶ categorized according to Stemper (2013).¹⁷ The colors correspond to Table 1.

weight, and women in the fourth quartile are overweight or obese.

Of our 654 records, 47 had to be omitted due to being incomplete regarding age, BMI, or WHtR, respectively. Thus, data from 607 patients could be analysed. The baseline characteristics of these 607 LiDo patients are summarized in Table 3.

According to the WHtR-categorization in Table 1, 15.2% of our LiDo patients were underweight, 45.5% were normal weight, 22.1% were overweight, and 17.3% were obese (grade I: 15.0%; grade II: 2.3%) (Table 4).

Figure 2 shows the distribution of the WHtR categories according to age groups. A chi-square test of independence was performed to examine the relationship between the WHtR category and the age group. The association between these variables was significant, χ^2 (20, $n = 607$) = 64.91, $p = 0.000$. We found underweight LiDo patients in all age groups. Throughout all age groups, more than 45% of the patients were normal weight. Overweight patients contributed to about a quarter of the age group 18–30, with lower percentages in the higher age groups, except for age group 61–70, where about a third of the patients were overweight. Patients with obesity grade I show peaks in the age group 31–40 (23.0%), age group 61–70 (18.0%), and age group > 70 (16.7%). In addition, very obese patients (grade II; $n = 14$) could be found only in the age groups 18–30, 31–40, 41–50, and 51–60.

In comparison with the general German data,¹⁶ our patients' median values of the WHtR are higher in all age groups (Figure 3). The 41–50 and 61–70 age groups are even in the overweight range. However, with a few exceptions (maximum values in age groups 31–40 and 51–60; minimum values in age groups 41–50 and 51–60), all our values are within the previously reported ranges of German women.¹⁶

When using the "traditional" BMI-categorization, 18.5% of the patients were normal weight, 30.3% overweight and 51.2% obese (grade I: 24.1%, grade II: 16.1%, grade III: 11.0%) (Table 4).

TABLE 3 Baseline characteristics of the LiDo patients.

n = 607	Mean	Median	SD	95% Confidence Interval	
				Lower limit	Upper limit
Age [yrs]	43.17	43.00	13.21	42.12	44.22
Weight [kg]	84.04	81.00	18.59	82.56	85.53
Height [cm]	164.24	164.00	6.89	163.63	164.73
Waist [cm]	86.82	85.00	13.84	85.71	87.92
BMI [kg/m ²]	31.18	30.10	6.81	30.64	31.73
WHtR	0.53	0.52	0.09	0.52	0.54

TABLE 4 Crosstab WHtR-categories vs. BMI categories.

		Body Mass Index					Total
		Normal weight	Overweight	Obesity			
				Grade I	Grade II	Grade III	
Waist-to-Height-Ratio	Underweight	54 (8.9%)	35 (5.8%)	2 (0.3%)	1 (0.2%)		92 (15.2%)
	Normal weight	56 (9.2%)	119 (19.6%)	74 (12.2%)	27 (4.4%)		276 (45.5%)
	Overweight	2 (0.3%)	26 (4.3%)	56 (9.2%)	36 (5.9%)	14 (2.3%)	134 (22.1%)
	Obesity Grade I		4 (0.7%)	13 (2.1%)	33 (5.4%)	41 (6.8%)	91 (15.0%)
	Obesity Grade II			1 (0.2%)	1 (0.2%)	12 (2.0%)	14 (2.3%)
	Total	112 (18.5%)	184 (30.3%)	146 (24.1%)	98 (16.1%)	67 (11.0%)	607 (100.0%)

$$\chi^2 (16, n = 607) = 469.60, p = 0.000$$

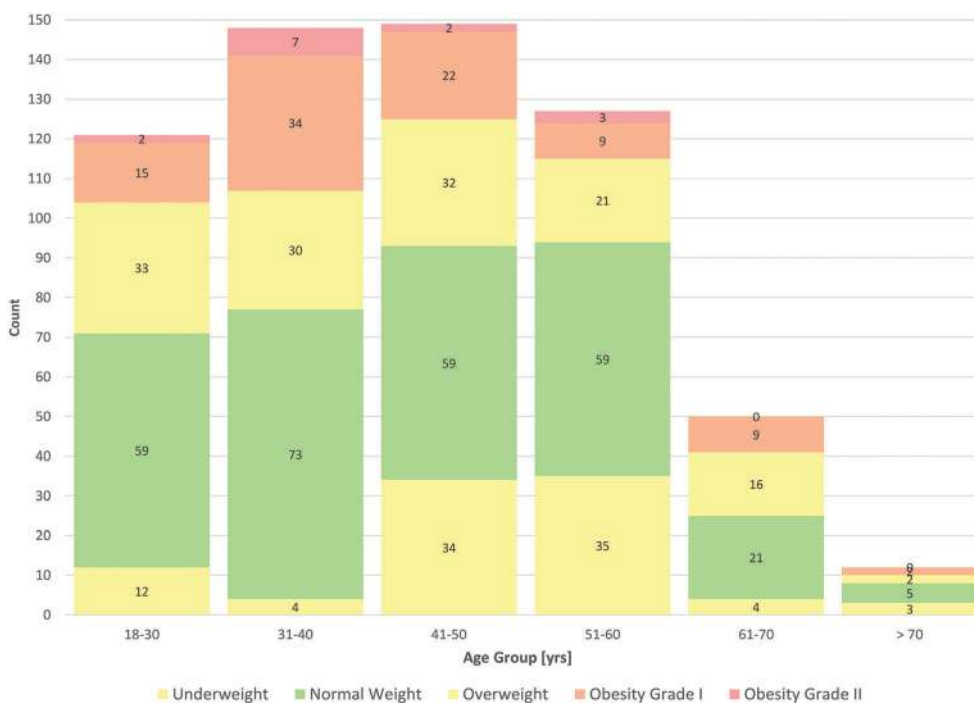
**FIGURE 2** WHtR categories by age-groups in 607 LiDo patients. The colors correspond to Table 1.

Table 5 shows the distribution of LiDo patients across the quartiles reported for a large German population broken down by age groups.¹⁶ It indicates that LiDo patients are similar (Q1: 22.1%, Q2: 23.1%, Q3: 27.9%, and Q4: 26.9%). However, the patients are somewhat heavier than the control group we chose.

Figure 4 reveals all the shifts between the BMI and WHtR categories. For instance, the 92 patients underweight according to WHtR include 54 normal weight (BMI), 33 overweight (BMI), and three obese patients. The 276 normal-weight patients according to WHtR include normal weight to grade II obese patients according to BMI.

FIGURE 3 WHtR quartiles of the current study vs. Schneider et al. (2010).¹⁶

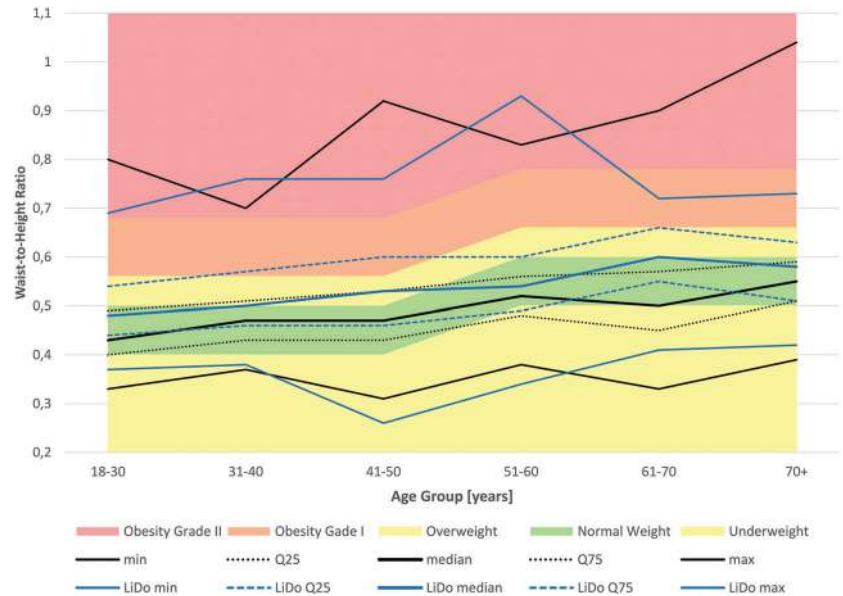
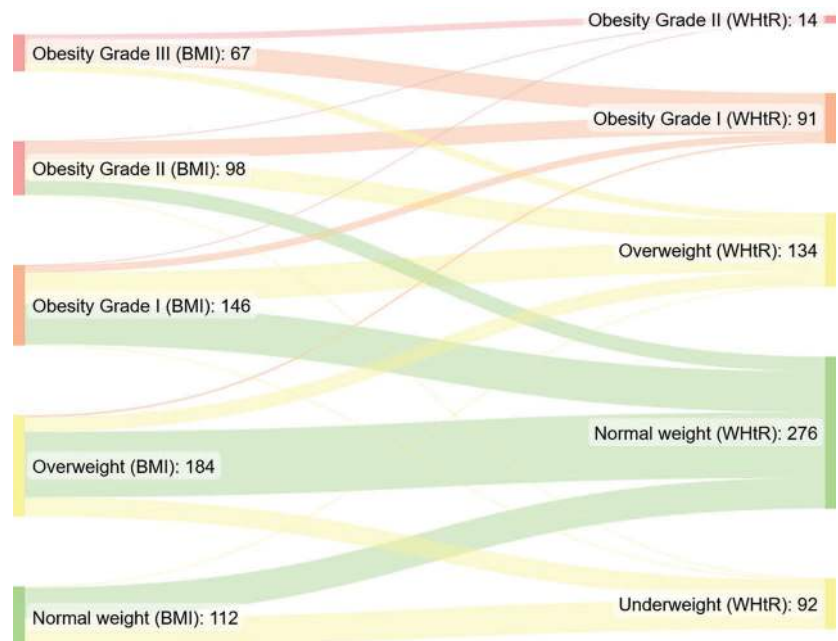


TABLE 5 Distribution of LiDo patients according to the interquartile ranges reported by Schneider et al. (2010).¹⁶

		Age-group						Total
		18-30	31-40	41-50	51-60	61-70	> 70	
Quartile	Q1	<i>0.33-0.40</i> 45 (7.4%)	<i>0.37-0.43</i> 34 (5.6%)	<i>0.31-0.43</i> 29 (4.8%)	<i>0.38-0.48</i> 15 (2.5%)	<i>0.33-0.45</i> 2 (0.3%)	<i>0.39-0.51</i> 3 (0.5%)	128 (21.1%)
	Q2	<i>0.40-0.43</i> 28 (4.6%)	<i>0.43-0.47</i> 43 (7.1%)	<i>0.43-0.47</i> 37 (6.1%)	<i>0.48-0.52</i> 24 (4.0%)	<i>0.45-0.50</i> 4 (0.7%)	<i>0.51-0.55</i> 2 (0.3%)	138 (22.7%)
	Q3	<i>0.43-0.49</i> 34 (5.6%)	<i>0.47-0.51</i> 38 (6.3%)	<i>0.47-0.53</i> 42 (6.9%)	<i>0.52-0.56</i> 43 (7.1%)	<i>0.50-0.57</i> 13 (2.1%)	<i>0.55-0.59</i> 2 (0.3%)	172 (28.3%)
	Q4	<i>0.49-0.80</i> 14 (2.3%)	<i>0.51-0.80</i> 33 (5.4%)	<i>0.53-0.92</i> 41 (6.8%)	<i>0.56-0.83</i> 45 (7.4%)	<i>0.57-0.90</i> 31 (5.1%)	<i>0.59-1.04</i> 5 (0.8%)	169 (27.8%)
Total		121 (19.9%)	148 (24.4%)	149 (24.5%)	127 (20.9%)	50 (8.2%)	12 (2.0%)	607 (100.0%)

Italic Numbers: Interquartile Ranges according to Schneider et al. (2010)¹⁶
 $\chi^2 (15, n = 607) = 76.16, p = 0.000$

FIGURE 4 Sankey diagram of BMI vs. WHtR. The colors correspond to Table 1.



DISCUSSION

Limitations of the study

This study is a retrospective study of patients previously diagnosed with LiDo. Although we are relatively certain that the diagnosis for all included patients is indeed LiDo, it cannot be ruled out with absolute certainty that in a few cases patients without LiDo but with lipohypertrophy were also included.

Body Mass Index

The unfortunate use of BMI in connection with LiDo means that many patients receive the devastating diagnosis of obesity and the therapy recommendation to lose weight. However, since LiDo is not a disease that can be cured with dietary measures, a vicious circle is created, and the patients' frustration increases. They are told that they are fat, but they cannot reduce this extra weight by dieting. At worst, bariatric surgery is performed, but this does not cure LiDo either, as LiDo-related pain does not change with bariatric surgery.²⁵

Moreover, obesity is already pandemic.²⁶ Obesity can affect women without and with LiDo. There is no causal connection between these diseases; at best, they occur coincidentally. Thus, for LiDo patients with coincident obesity, the increase in SAT of the extremities is composed of both a LiDo component and an obesity component. However, in such patients, diets and bariatric surgery do result in weight loss and volume reduction, including on the LiDo extremities. The patients are then told that the diet or surgery was successful and that all they have to do is continue the therapy with as much effort as possible. Although it is possible that patients may reduce their obesity related SAT even further, the LiDo portion remains. The LiDo portion can be reduced by liposuction, which reduces not only the excessive volume but also the perceived pain.^{27,28}

This dilemma also affects the recent decision of the G-BA on the reimbursement of costs for liposuction through health insurance funds.⁹ Patients with a BMI of more than 40 kg/m², i.e., with obesity grade III, are de facto excluded from cost coverage. This would affect 67 patients (11.0%) from our cohort, of whom 14 are "only" overweight according to WHtR. Patients with a BMI between 35 kg/m² and 40 kg/m², i.e., obesity grade II, must at least receive conservative obesity therapy before they can undergo reimbursed liposuction. In our study, 98 patients (16.1%) are in this group, of whom 27 (4.4%) are of normal weight according to WHtR and another 36 are overweight (5.9%). It can be assumed that (conservative) obesity therapy is insufficient in the 27 normal-weight patients and that these patients are therefore wrongly excluded from liposuction; in the 36 overweight patients, such treatment could at least be partially effective, so that liposuction is possible after all. The use of WHtR could therefore be a constructive argument here.

Another problem of coincident obesity is obesity-associated lymphatic dysfunction.²⁹ In many cases, this disorder manifests itself as obesity-associated lymphedema. However, some classifications incorrectly assign this lymphedema to "LiDo" disease as stage 4 (lipolymphedema).

In LiDo, however, lymphatic function is not impaired. Still, it is known that young LiDo patients have an increased transport function of the lymphatic vascular system compared to the general, healthy population. In contrast, older patients have a reduced transport function.³⁰ These findings indicate an increased lymphatic water load in young LiDo patients with initially sufficient, and with increasing age decreasing adaptation of, lymphatic transport. Since neither the stage of LiDo nor the BMI was correlated with lymphatic transport in this study, the decrease in lymphatic transport with increasing age could also be attributed to coincident obesity, which becomes more likely with older age. Lymphoscintigraphic alterations were found in 47% of LiDo patients, most of which were considered low grade or low-moderate grade. The presence of this dysfunction did not correlate with age or BMI,³¹ but with the duration of symptoms.³²

Waist-to-Height Ratio

Bertsch et al.³³ concede that patients with LiDo and a WHtR < 0.5 are probably not at metabolic risk,^{16,34,35} so "bariatric surgery is not absolutely necessary". According to Schneider et al.¹⁶, a cut-off value of 0.5 for patients up to 40 years of age and 0.6 for patients 50 years of age and older seems to provide a reasonable estimate of the future risk of death and cardiovascular events; for the age group between 40 and 50 years, the cut-off values are between 0.5 and 0.6. Stemper¹⁷ suggested that the cut-off value should be increased by 0.01 per year between 40 and 50 years of age.

Therefore, it is surprising that only one study on this parameter in LiDo has been published.³⁶ However, in this study, Herpertz uses the Nauheimer obesity scale he developed.³⁷ We thus present what is probably the first study worldwide to examine WHtR exclusively in patients with LiDo.

In our patients, WHtR increases with age but is only significantly above the threshold in young patients (< 40 years). However, this increase corresponds to the (German) control group.¹⁶ Our data are within the range of this population with some minimal exceptions. Nevertheless, the distribution of the WHtRs of our LiDo patients according to the quartiles of a large German population¹⁶ is quite interesting. There are fewer patients in the first quartile of this control group (21.1%), whereas the other quartiles show higher percentages (Q2: 22.7%, Q3: 28.3%, Q4: 27.8%, respectively). This means that the distribution of LiDo patients is in line with the distribution of German women in general.

Of course, our categorization of LiDo patients as "underweight", "normal weight", "overweight", or "obese" only considers the ratio between waist circumference and body height, i.e., the mass of abdominal subcutaneous and

visceral fat tissue. However, the disproportionate excess of SAT in the extremities could also be a factor in metabolic and/or cardiovascular risk. However, Faerber⁸ found in her studies that insulin resistance was less pronounced in a collective of obese LiDo patients than in a comparative collective of obese patients without LiDo, despite a higher average weight, although this difference was lost with increasing abdominal obesity. The SAT of LiDo patients seems not to promote metabolic disease.^{5,7}

CONCLUSIONS

In LiDo, the exclusive use of BMI not only overestimates metabolic risks, but, due to the disproportionate distribution of SAT, may also lead to a misdiagnosis of obesity. Thus, using BMI to evaluate LiDo patients may lead to inappropriate and unnecessary obesity treatment. Therefore, to assess or exclude obesity, we suggest using WHtR. If both BMI and WHtR are used, a normal WHtR with increased BMI indirectly indicates a disproportionate increase in SAT. Neither BMI nor WHtR nor course are tools to diagnose LiDo.

CONFLICT OF INTEREST

None.

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How to cite this article: Brenner E, Forner-Cordero I, Faerber G, Rappich S, Cornely M. Body mass index vs. waist-to-height-ratio in patients with lipohyperplasia dolorosa (vulgo lipedema). *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*. 2023;21:1179–1185.
<https://doi.org/10.1111/ddg.15182>