Muscle strength and functional functional exercise capacity in patients with lipedema and obesity: a pilot study

Master thesis

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ONDERGETEKENDE

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bevestigt hierbij dat de onderhavige verhandeling mag worden geraadpleegd en vrij mag worden gefotokopieerd. Bij het citeren moet steeds de titel en de auteur van de verhandeling worden vermeld.”

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Samenvatting

Rationale: Lipoedeem is een afwijking van vetweefsel die alleen voorkomt bij vrouwen, vaak verkeerd gediagnosticeerd als lymfoedeem of obesitas. Bij het meten van spierkracht wordt vaak een verminderde spierkracht gevonden bij patiënten met lipoedeem vergeleken met normwaarden. Het meten van spierkracht en functionele inspanningscapaciteit kan helderheid geven om te kunnen differentiëren tussen lipoedeem en obesitas. Ondanks klinische observatie bij patiënten met lipoedeem, is de spierkracht nog nooit wetenschappelijk onderzocht bij patiënten met lipoedeem. Het primaire doel van deze studie is onderzoeken of er een verschil is in spierkracht tussen vrouwen met lipoedeem en vrouwen met obesitas. Het secundaire doel van deze studie is onderzoeken of er een verschil is in functionele inspanningscapaciteit tussen vrouwen met lipoedeem en vrouwen met obesitas.

Methode: Het betreft een cross-sectionele pilot studie. In totaal zijn 44 vrouwen geïncludeerd. Tweeëntwintig vrouwen met lipoedeem en 22 vrouwen met obesitas. Deelnemers werden geïncludeerd in de lipoedeemgroep wanneer ze voldeden aan de volgende criteria: 1) gediagnosticeerd met lipoedeem volgens de criteria van Wold *et al.*; 2) ≥18 jaar. Deelnemers werden geïncludeerd in de obesitasgroep wanneer ze voldeden aan de volgende criteria: 1) Body Mass Index ≥ 30; 2) vrouwelijk geslacht; 3) ≥ 18 jaar. Spierkracht van de m. quadriceps werd gemeten met de MicroFET en functionele inspanningscapaciteit werd gemeten met de zes minuten wandeltest (6MWT). Een independent samples t-test werd uitgevoerd om verschillen in spierkracht en fysiek uithoudingsvermogen tussen de beide groepen aan te tonen.

Resultaten: Patiënten met lipoedeem hadden een statistisch significant ($p<0.01$) lagere spierkracht van de m. quadriceps voor beide benen vergeleken met patiënten met obesitas. Patiënten met lipoedeem scoorden 494.1(±116.0) m en patiënten met obesitas scoorden 523.9(±62.9) m op de 6MWT. Dit verschil is niet statistisch significant ($p=0.296$).

Conclusie: Patiënten met lipoedeem hebben een verminderde kracht van de m. quadriceps vergeleken met patiënten met obesitas. Gezien deze verschillen, kan het meten van spierkracht bij patiënten met lipoedeem gebruikt worden als aanvulling op het standaard klinisch onderzoek. Daarnaast kan het gebruikt worden als mogelijke ingang voor therapie.

Keywords (max 5): Lipedema, overweight, muscle power, physical endurance, women

Abstract

Rationale: Lipedema is a disorder of adipose tissue that occurs exclusively in women, frequently misdiagnosed as lymphedema or dismissed as obesity. It is often seen that muscle strength is decreased in patients with lipedema compared to norm values. Measuring muscle strength and functional exercise capacity may give more clarity to differentiate between lipedema and obesity. Although investigated in many patients, this has never been examined in a scientific study. The primary aim of the current study is to investigate whether there is a difference in muscle strength between women with lipedema and women with obesity. The secondary aim of the current study is to investigate whether there is a difference in functional exercise capacity between women with lipedema and women with obesity.

Methods: The current study is a cross-sectional pilot study. Forty-four women of 18 years and older participated in this study. Twenty-two women with lipedema and 22 women with obesity. Participants were included in the lipedema group when they were: 1) diagnosed with lipedema following the criteria of Wold *et al*.; 2) age ≥18 years. Participants were included in the obese group when they met the following criteria: 1) Body Mass Index ≥30; 2) female; 3) age ≥18 years. Muscle strength of the m. quadriceps was measured with de MicroFET and functional exercise capacity was measured with the six minute walking test (6MWT) in women with lipedema and women with obesity. Independent samples t-tests were performed to determine differences in muscle strength and functional exercise capacity between women with lipedema and women with obesity.

Results: Patients with lipedema had statistically significant (p=0.00) lower muscle strength of the m. Quadriceps compared to patients with obesity for both legs. Patients with lipedema scored 494.1(±116.0) m and patients with obesity scored 523.9(±62.9) m on the 6MWT. The difference in functional exercise capacity was not statistically significant (P=0.296).

Conclusion: There is a negative difference in muscle strength between patients with lipedema and patients with obesity. Considering these differences in muscle strength, measuring muscle strength in patients with lipedema is recommended to be added to the standard clinical examination. Moreover a possible entry for exercise training.

Keywords (max 5): Lipedema, overweight, muscle power, physical endurance, women

Introduction

Lipedema is a disorder of adipose tissue that occurs almost exclusively in women (1-3). It is a chronic, progressive condition, that is associated with considerable morbidity (4). Characteristics of lipedema are swelling and enlargement of the lower limbs due to abnormal deposition of subcutaneous fat. It is an under-recognized condition, often misdiagnosed as lymphedema or dismissed as obesity (1). Lipedema is probably attributable to an autosomal dominant inheritance with sex limitation (1).

The prevalence of lipedema in women is not known exactly. In 2001 Földi & Földi concluded that lipedema is present in 11% of the general female population (5). Lipedema is normally first noticed at puberty, pregnancy of menopause (6). To make a reliable clinical diagnosis, it is important to differentiate between disorders that present with swelling and fat deposits (1-4). In table 1 the differential diagnosis of lipedema are described, such as lipohypertropy, lymphedema and (morbid) obesity (3). In 1951, Wold *et al*.(3) proposed a set of diagnostic criteria for lipedema (4).

There are two major phenotypes of lipedema defined: columnar and lobar (7,8). Both phenotypes can develop in an ascending or descending fashion. The columnar seems to be predominant (4,9-12) and can be described as enlargement of proportions of the lower extremities as a series of varying conic sections. The less common lobar type is typified by the presence of large buges or lobes of adipose tissue that overlay enlarged lower extremities or hips (4,12). Combination or hybrid presentations of both types can occur (2).

The International Classification of Functioning, Disability and Health (ICF) (13) introduced participation as an interesting outcome measure of health. The ICF is a multipurpose classification for the description of health and health-related states, and defines participation as ‘involvement in life situations’ (13). In addition to physical problems, lipedema may be associated with psychological morbidity (14). Additional feelings of embarrassment and social disgrace can lead to depression, reluctance in participation and eventually social isolation (14). Although non-curative in nature and still in their infancy, treatment options such as physical therapy regarding lipedema can relief patients from severe mechanical limitations in everyday

life, and provide strategies for coping with the chronic condition and all its consequences (14). Therefore, it is important that lipedema is recognized as early as possible and that patients receive optimal information and care (1,4).

Table 1. Diagnostic aids in the differential diagnosis of lipedema; lipohypertrophy; lymphedema and obesity

Characteristics	*Lipedema*	*Lipohypertrophy*	*Lymphedema*	*Obesity*
Sex	Female	Female	Males and females	Female dominance
Age of onset	Puberty	Puberty	Any decade	Any decade
Family history positive	In approximately 15% of cases	Possible	In approximately 20% twin of primary LE	65% based on studies
Proven heredity factor	Absent	Absent	Primary LE	Absent
History of erysipelas	Absent	Absent	Usually	Absent
Effect of diet	None	None	None	Excellent
Effect of elevation	Minimal (limited to pitting component)	Initially effective	Initial effective	Ineffective
Physical examination				
Bilateral	Always	Always	Primary: often Secondary: seldom	Always (android of gynoid*)
Involvement feet	Absent	Absent	Common	Common
Pitting edema	Absent (initially)	Absent	Present	Absent
Retromalleolar fat pad	Present	Absent	Absent	Absent
Consistency on palpation	Soft-firm	Soft	Firm	Soft
Easy bruising of affected skin areas	Common	Absent	Absent	Absent
Tenderness of affected skin areas	Common	Absent	Absent	Absent
Stemmer's sign	Absent	Absent	Present	Absent

Table 1:adapted from tables proposed by Wold et al.(3), Langendoen et al.(4), Child et al.(1) and Fife et al.(2). *Android; centralized or "apple-shaped" obesity; gynoid; generalized or "pear-shaped" obesity.

Treatment of lipedema can be conservative and/or surgical of nature, the latter reserved for lipedema non-responsive to conservative treatment or severe mechanical restrictions in everyday life (14). A combination of skin care, manual lymphatic therapy, compression therapy and physical exercise provides efficacious edema reduction (15). Increasing muscle power, re-activation and re-conditioning of the patient combined with increasing of a healthy lifestyle and quality of life (QoL) may be essential parts of the conservative treatment (14). Physical therapy is aiming at increasing muscle power, increasing a healthy lifestyle, QoL and providing proper body use and movement (14). Effect of therapy is objectified by means of measuring muscle strength of the upper leg (m. quadriceps) as a guideline for overall condition (14).

Patients with lipedema often have an elevated Body Mass Index (BMI) (1). However, while obesity will respond to restricted dietary intake, lipedema component will not or partially, leading to a wasted upper body and a lower body that stubbornly remains the same shape from the waist to the ankles (1). Clinical examination may show loss of muscle strength in patients with lipedema compared to healthy or obese persons, however this is never examined in a scientific study (2). In the Expertise Centre for Lymphology in Nij Smellinghe Drachten, a lot of patients with lipedema are seen every year. Patients suffer from fatigue and loss of muscle strength. Muscle strength is often seen to be decreased in patients with lipedema compared to norm values. Functional exercise capacity is also measured, since exercise is associated with QoL (14).

The diagnosis lipedema is mainly made on clinical and anamnestic soils. Validated criteria to support or reject the diagnosis are not available. Besides volumetry, BMI and pain score, measuring muscle strength may give more clarity to differentiate between lipedema and obesity. This may lead to improvements in the criteria for diagnosing lipedema and become part of the health profile leading to an entrance in therapy. Therefore, the research question of the current study is: is there a difference in muscle strength between women with lipedema and women with obesity? In addition, a secondary research question is proposed: is there a difference in functional exercise capacity between women with lipedema and women with obesity? It is hypothesized that there is a difference between muscle strength and functional exercise capacity between women with lipedema and women with obesity.

Patients & Methods

Study design

This study was a cross-sectional pilot study performed in Nij Smellinghe Hospital Drachten, the Netherlands from February 2013 till April 2013. Data of the lipedema group was collected retrospective by medical file study. All measurements were part of usual care for this group. Data of the obesity group was collected prospectively. The medical ethics committee (MEC) of Nij Smellinghe Hospital approved the study and all patients gave signed informed consent.

Patients

Adult patients with lipedema or obesity were recruited for participation in the current study. The participants of the lipedema group were already in treatment in Nij Smellinghe Hospital. Medical files of the lipedema participants were used to complete the data. Thus patients in the lipedema group did not perform supplementary tests. The participants in the obesity group were recruited and measured in 2013. The recruitment was performed by dermatologists and physical therapists of Nij Smellinghe Hospital from the regular work load. Participants were included in the lipedema group when they were: 1) diagnosed with lipedema following the criteria of Wold *et al*.(3); 2) age ≥18 years. Participants were included in the obese group when they met the following criteria: 1) BMI ≥30; 2) female; 3) age ≥18 years. There were no exclusion criteria for the lipedema group. Participants in the obese group were excluded if they participated in an obesity training program ≤12 months prior to the measurement moment.

Study parameters

Prior to the measurement, the researcher (JS) collected the demographic characteristics age (years), and anthropometric characteristics height (cm), weight (kg) and BMI (kg/m^2) of all participants. Data collected in the obesity group was collected following a standardised protocol. Collected data in the lipedema group was part of usual care, following a standardised protocol. These measurements were performed by several trained physical therapists of Nij Smellinghe Hospital. The primary outcome parameter was the strength of the quadriceps muscle of the left and right leg measured with the MicroFET using the break-method (16). Muscle strength of the m. quadriceps is measured as a guideline for overall muscle condition (17).
The test was performed by JS when the participant was sitting in a chair with crossed arms.

The participant was instructed to perform knee extension three times with each leg. The test result in Newton (N) is the highest score of each leg (18). The MicroFET had been shown a valid measurement with the break-method (14,15). Schaubert *et al.*(18) and Bohannon *et al.*(16) found high intraclass correlation coefficient (ICC) values of the MicroFET measurements of 0.807-0. 971 (18) and ICC>0.970 (16) respectively. Data of each leg of each participant were compared to norm values (19).

The secondary outcome parameter of the current study was functional exercise capacity measured with the six minute walk test (6MWT) (20). This standardized test is performed on a 30-meter course where every five meter is marked. The test was performed by JS. The patient was instructed to cross a maximum distance in six minutes with the possibility to stop or rest if necessary (20). During the test, the participant was encouraged to walk as far as possible (16,21). The result is the walking distance in meters (m) after six minutes (with five meter exactness). The test-retest reliability of this test is high (ICC 0.94) in older adults (22). The walking distance (m) of each participant was compared to norm values of healthy subjects (21).

Analyses

All data were analyzed with the statistical package for social sciences (SPSS) version 20.0. Tests for normality were performed on the data with the Shapiro-Wilk test. All data were normally distributed. Data were presented as quantitative data and expressed as mean ± standard deviation (SD). Demographic and anthropometric data were described using descriptive statistics. Independent samples t-tests were used to compare women with lipedema and women with obesity, concerning muscle strength and functional exercise capacity. This test was also used to compare measured values to norm values. An alpha of 0.05 was considered statistically significant.

Results

Study population

In total, 44 participants were included in the study. Twenty-two participants were diagnosed with lipedema (lipedema group) and 22 participants were diagnosed with obesity (obesity group). The mean age of the participants was 43.8±12.4 years (lipedema group 39.2±13.0 years; obesity

group 48.5±9.9 years). The mean BMI was 34.3±6.5 kg/m^2 (lipedema group 33.59±8.3 kg/m^2; obesity group 35.06±4.3 kg/m^2). All demographic and anthropometric data are described in table 2. All participants performed a MicroFET measurement and a 6MWT without any complications or adverse events.

Table 2. Demographic data of the study population

Variable	*Total group (n=44)*	*Lipedema group (n=22)*	*Obesity group (n=22)*
Age (years), mean (SD)	43.8 (12.4)	39.23 (13.0)	48.45 (9.9)
BMI (kg/m^2), mean (SD)	34.33 (6.5)	33.59 (8.3)	35.06 (4.3)

SD, standard deviation; BMI, body mass index

Muscle strength

Table 3 presents the mean scores of the muscle strength measurements of both groups. The mean score of the lipedema group was 269.7±67.8 N for the right leg and 259.9±77.3 N for the left leg. The obesity group scored 400.3±69.1 N for the right leg and 401.5±75.9 N for the left leg. There is a statically significant difference in muscle strength between the lipedema and obesity group for the right ($p<0.01$) and left leg ($p<0.01$). The lipedema group scored much lower than the obesity group. Participants with lipedema scored of 67.0±22.9% (right) predicted and 67.7±19.1% (left) of predicted compared to norm values of healthy women. Participants with obesity scored 100.0±20.4% and 103.6±20.9% of predicted respectively.

Functional exercise capacity

Table 3 also presents the mean scores of the 6MWT of both groups and the results of the Independent Samples T-test. The mean score for de lipedema group was 494.1±116.0 m, the obesity group scored 523.9±62.9 m. There was no statistically significant difference between the groups ($p=0.296$). Compared to norm values of healthy people, no statistically significant difference ($p=0.071$) was found between the groups, when the distance covered was expressed as a percentage of predicted.

Table 3. Mean scores and comparison of the MicroFET measurements and the 6MWT for the lipedema and obesity group.

	Lipedema group (n=22)	Obesity group (n=22)	p-value
Muscle strength m. quadriceps right (N), mean(SD)	269.7 (67.8)	400.3 (69.1)	<0.01
Muscle strength m. quadriceps right as % of norm value, mean (SD)	67.7 (19.1)	100.0 (20.4)	<0.01
Muscle strength m. quadriceps left (N), mean (SD)	259.9(77.3)	401.5 (75.9)	<0.01
Muscle strength m. quadriceps left as % of norm value, mean (SD)	67.0 (22.9)	103.6 (20.9)	<0.01
6MWT (meters), mean (SD)	494.1(116.0)	523.9 (62.9)	0.296
6MWT as % of norm value, mean (SD)	92.1 (23.6)	102.4 (11.0)	0.071

N, Newton; SD, standard deviation; 6MWT, six minute walk test; norm values MicroFET by Andrews *et al.*(19)*;* norm values 6MWT test by Enright *et al.*(21)

Discussion

The primary aim of the present study was to investigate whether there is a difference in muscle strength between women with lipedema and women with obesity. The results show that there is a statistically significant difference in muscle strength between women with lipedema and obesity. A difference is also seen in percentage of the predicted score, where participants with lipedema show a decreased m. quadriceps muscle strength up to 30%, while patients with obesity showed 103.6% of predicted. The secondary aim was to investigate whether there is a difference in functional exercise capacity between women with lipedema and women with obesity. Considering the secondary aim, a small, not statistically significant, difference in favor of the obesity group is seen in functional exercise capacity between women with lipedema and obesity, with lower values obtained by the lipedema group.

The results of the present study are relevant since muscle strength was not investigated previously in patients with lipedema. In its early stage of development, lipedema, can cause complaints of discomfort without any obvious enlargement of the extremities upon physical examination (14). The course of decreased muscle power in patients with lipedema is still unknown. Information about muscle strength, compared to norm values in patients with lipedema may give more clarity in the severity of the disease during physical examination and in early stages of lipedema, as well as a possible input for physical therapy considering muscle strength. The functional exercise capacity shows a small difference between both groups. Compared to norm values the lipedema group scored 92% of predicted compared to 102% of predicted in the obesity group. Although the differences are small, this may be explained by the sources of variability set by the American Thoracic Society (ATS) (23). The ATS named muscle wasting as one of the reducing factors in performing the 6MWT (23). Since patients with lipedema suffer from muscle weakness, this also may be a reducing factor in performing the 6MWT. Buchner *et al.*(24) first recognized a non-linear relationship between leg strength and usual gait speed; this relationship explained how small changes in physiological capacity may have substantial effects on performance in frail adults, while large changes in capacity have little or no effect in healthy adults. This mechanism may also be applicable in patients with lipedema.

Lipedema is a chronic condition with the possibility to aggravate during life when no life style change is made. The incurable course and severity of findings depend to a large extent of co morbidities such as obesity and psychological and/or psychiatric disorders (25). The cause of lipedema is still unknown, no curative therapy is known (6). The goal of treatment is therefore improvement of the subjective symptoms and prevention of progression of lipedema (26). Unfortunately, many patients are uncertain about the amount of physical activity they can undertake. Some patients think that activity will lead to increased muscle mass in the legs, increasing the disproportion between upper and lower body even more (27). Physical activity should be encouraged for patients with lipedema. Exercise also activates pump function in the lower limb muscles, reducing edema formation in the tissue and reduces the risk of additional obesity (26). With presently available therapy options, cure is not possible, but the patient can positively impact the course by her compliance (26). Women who consistently wear their compression stockings and maintain normal weight, usually have a distinctly better prognosis and

a milder course than those, who in addition to existing lipedema, are obese and do not exercise or take part in sporting activity (26).

In the present study, the 6MWT is used to measure functional exercise capacity. Other studies, measuring functional exercise capacity in women with obesity use an electronically braked cycle ergometer to determine peak oxygen uptake (28). In the Expertise Centre for Lymphology the 6MWT is used because it is a practical and valuable measurement, since most patients with lipedema experience difficulties in walking. The MicroFET was used to examine muscle strength. The MicroFET is less expensive and more efficient than isokinetic dynamometry for providing quantitative measurements of the isometric force of muscle actions (19). A limitation of the study is the considerable experience of the testers. Whether less experienced examiners will be able to obtain similar levels of reliability is not known (19).

To our knowledge, the present study is the first study that investigated muscle strength and functional exercise capacity in patients with lipedema. So far, there was no knowledge available on the methodology of measuring physical fitness in this group. The chosen measurements in this study are part of usual care in Nij Smellinghe Hospital for patients with lipedema. A limitation of the study was the absence of a standardized protocol used for the measurements in the lipedema group. There is a test protocol available, but application of this protocol may be achieved slightly different by the several physical therapists who treat patients with lipedema. Another limitation of this study was the small sample size in both groups; however this was a pilot study. Consequently the results of this study should be interpreted with taking these limitations into account. Further research is needed to show if a decreased difference in muscle strength in patients with lipedema compared to norm values can be used as a supplementary criterion in diagnosing lipedema and if they are suitable as therapeutic parameters to measure the success of treatment. The literature suggests that muscle training has positive effects on lipedema considering the increase of the pump function of the lower limb muscles (26). Further research should be done considering the effects of muscle training of the legs, in example the m. quadriceps in patients with lipedema.

Conclusion

There is a statistically significant difference in muscle strength, whereas there was no statistically significant difference in functional exercise capacity between women with lipedema and women with obesity. Considering these differences in muscle strength, measuring muscle strength in women with lipedema seems to be a good addition to the standard clinical examination, to set the diagnosis lipedema and a possible entrance for exercise training.

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