New Insights on Lipedema: The Enigmatic Disease of the Peripheral Fat

Anna-Theresa Bauer, M.D.
Dominik von Lukowicz, M.D.
Katrin Lossagk, M.D.
Matthias Aitzetmueller, M.D.
Philipp Moog, M.D.
Michael Cerny, M.D.
Holger Erne, M.D.
Daniel Schmauss, M.D., Ph.D.
Dominik Duscher, M.D.
Hans-Guenther Machens, M.D., Ph.D.

Munich, Germany; and Lugano, Switzerland

Background: Although a large number of adult women worldwide are affected by lipedema, the physiologic conditions triggering onset and progression of this chronic disease remain enigmatic. In the present study, a descriptive epidemiologic situation of postoperative lipedema patients is presented.

Methods: The authors developed an online survey questionnaire for lipedema patients in Germany. The survey was conducted on 209 female patients who had been diagnosed with lipedema and had undergone tumescent liposuction.

Results: Most of the participants (average age, 38.5 years) had noticed a first manifestation of the disease at the age of 16. It took a mean of 15 years to accomplish diagnosis. Liposuction led to a significant reduction of pain, swelling, tenderness, and easy bruising as confirmed by the majority of patients. Hypothyroidism [n = 75 (35.9 percent) and depression [n = 48 (23.0 percent)] occurred at a frequency far beyond the average prevalence in the German population. The prevalence of diabetes type 1 [n = 3 (1.4 percent)], and diabetes type 2 [n = 2 (1 percent)] was particularly low among the respondents. Forty-seven of the lipedema patients (approximately 22.5 percent) suffered from a diagnosed migraine. Following liposuction, the frequency and/or intensity of migraine attacks became markedly reduced, as stated by 32 patients (68.1 percent).

Conclusions: Quality of life increases significantly after surgery with a reduction of pain and swelling and decreased tendency to easy bruising. The high prevalence of hypothyroidism in lipedema patients could be related to the frequently observed lipedema-associated obesity. The low prevalence of diabetes, dyslipidemia, and hypertension appears to be a specific characteristic distinguishing lipedema from lifestyle-induced obesity. (*Plast. Reconstr. Surg.* 144: 1475, 2019.)

Lipedema is a disease mainly affecting women. It is characterized by disproportional fat accumulation of the lower and also upper extremities that can result in considerable disability.[1] The hypertrophic fat pads normally extend from the hips to the ankles and/or from the shoulders to the wrists and are typically unresponsive to dietary regimens or physical activities.[2] In addition to the aesthetic deformity, women also describe pain in the lower extremities, which increases during the day, with tenderness, easy bruising, and progressive lymphedema.[3]

In many cases, mothers, grandmothers, sisters, and aunts are affected in a comparable way.[4] However, the genetic background of the disease has not been fully discovered yet.[5] A study from 2010 showed that within six families of more than three generations with lipedema, a genetic autosomal-dominant hereditary pattern was found.[6] Although the condition is well described, and an estimated 8 to 17 percent of adult women worldwide are affected, it is still often misdiagnosed and

From the Department of Plastic Surgery and Hand Surgery, Klinikum rechts der Isar, Technical University Munich; the Praxis Ästhetik in München, Dr. von Lukowicz und Kollegen; and the Division of Plastic, Reconstructive, and Aesthetic Surgery, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale.
Received for publication September 6, 2018; accepted March 28, 2019.

DOI: 10.1097/PRS.0000000000006280

Disclosure: *None of the authors has a financial interest to declare in relation to the content of this article. No funding was received for this work.*

A "Hot Topic Video" by Editor-in-Chief Rod J. Rohrich, M.D., accompanies this article. Go to PRSJournal.com and click on "Plastic Surgery Hot Topics" in the "Digital Media" tab to watch.

underrepresented in medical education.[7] Despite the strong impact of this disease on millions of women's lives, only limited research has been done on the topic of its pathophysiology.

Unlike obesity, the fat depots and swelling associated with lipedema are resistant to dietary changes, caloric intake restriction, exercise, or bariatric surgery.[8] One of the classic findings concerning lipedema is the relative sparing of the feet and hands. As if wearing a bracelet or anklet, the swelling and enlargement of the extremities ends at the wrists and ankles, comparable to a cuff.[7] Moreover, the vessel frailty of lipedema patients is reflected by easy bruising following inadequate traumata and pressure.[7] At advanced stages, some of the patients also develop lymphedema,[9] which makes correct diagnosis of lipedema even more difficult.

In this article, we present an epidemiologic study conducted on 209 female patients diagnosed with stage II lipedema and treated with liposuction. Using a comprehensive questionnaire focusing primarily on clinical symptoms and comorbidities, we aim to present a descriptive epidemiologic situation of postoperative lipedema patients.

PATIENTS AND METHODS

Study Design

We designed an online survey (SurveyMonkey, San Mateo, Calif.) consisting of 42 questions evaluating the preoperative and postoperative situation of lipedema patients. The survey was conducted on 209 patients who had been diagnosed with lipedema and had undergone tumescent liposuction. Respondents were recruited through their local lymphedema clinics, lipedema patient support groups, and plastic surgeons. Respondents had access to a Web link only through a restricted authorization group, ensuring a high percentage of correctly diagnosed lipedema patients.

Statistical Analysis

Statistics were carried out using Microsoft Excel 2010 (Microsoft Corp., Redmond, Wash.) calculating mean, median, and standard deviation. The t test was performed and a value of $p < 0.05$ was considered significant.

RESULTS

Lipedema Onset

The median age of 209 female lipedema patients was 38 ± 10 years. On average, liposuctions had been carried out 12 months before the survey. The oldest participant was aged 68 years and the youngest was aged 20 years. Next, the study sought to determine the average age at which respondents noticed signs of lipedema for the first time. The majority of the respondents [$n = 68$ (32.5 percent)] experienced first symptoms at the age of 14 to 18 years, followed by 57 (27.3 percent) and 33 patients (15.8 percent) who reported having noticed first symptoms at the age of 19 to 23 and 24 to 28 years, respectively. The most advanced age reported was 54 years. The mean age ± SD at which participants noticed lipedema symptoms for the first time was 16 ± 9 years (Fig. 1, *above*). We further asked how long the participants had lived with the disease before being diagnosed. The mean number of years before diagnosis was 15 ± 10. One of the respondents indicated having lived with the disease for 59 years until it was diagnosed. The shortest period until diagnosis was less than 1 year. Most of the respondents [$n = 43$ (20.6 percent)] reported having lived with the disease for 14 years, followed by 33 (15.8 percent) who reported 19 years before diagnosis (Fig. 1, *below*).

Surgical Treatment

The lowest number of operations conducted on lipedema patients was one, and the highest was 16. One hundred seventy-three respondents (82.8 percent) indicated they had four operations, and 24 respondents (11.9 percent) reported more than nine operations. Twelve respondents did not answer this question correctly. The average number of operations ± SD conducted was 3 ± 2 (Fig. 2, *above*). Next, we took a closer look at the exact areas treated by liposuction. Thighs, calves, buttocks, back, and abdomen were the areas mentioned by the participants. Women mentioned complete thighs [$n = 133$ (63.6 percent)], frontal parts of thighs [$n = 43$ (16.3 percent)], lateral thighs [$n = 37$ (17.7 percent)], backside of thighs [$n = 25$ (12.0 percent)], and inside of thighs [$n = 44$ (21.1 percent)]. Buttocks were mentioned by 71 respondents (34 percent), frontal calves by 125 respondents (59.8 percent), calves by 31 respondents (14.8 percent), upper arms by 101 respondents (48.3 percent), forearms by 59 respondents (28.2 percent), and finally back and abdomen by 24 (11.5 percent) and 29 respondents (13.9 percent), respectively (Fig. 2, *below*). The highest total amount of pure fat removed from a patient's body was 69 liters ($n = 1$), followed by 59 liters ($n = 2$). The lowest total amount of pure fat extracted was 9 liters, mentioned by 41.1 percent ($n = 86$), followed by 29 liters ($n = 74$). The average amount of

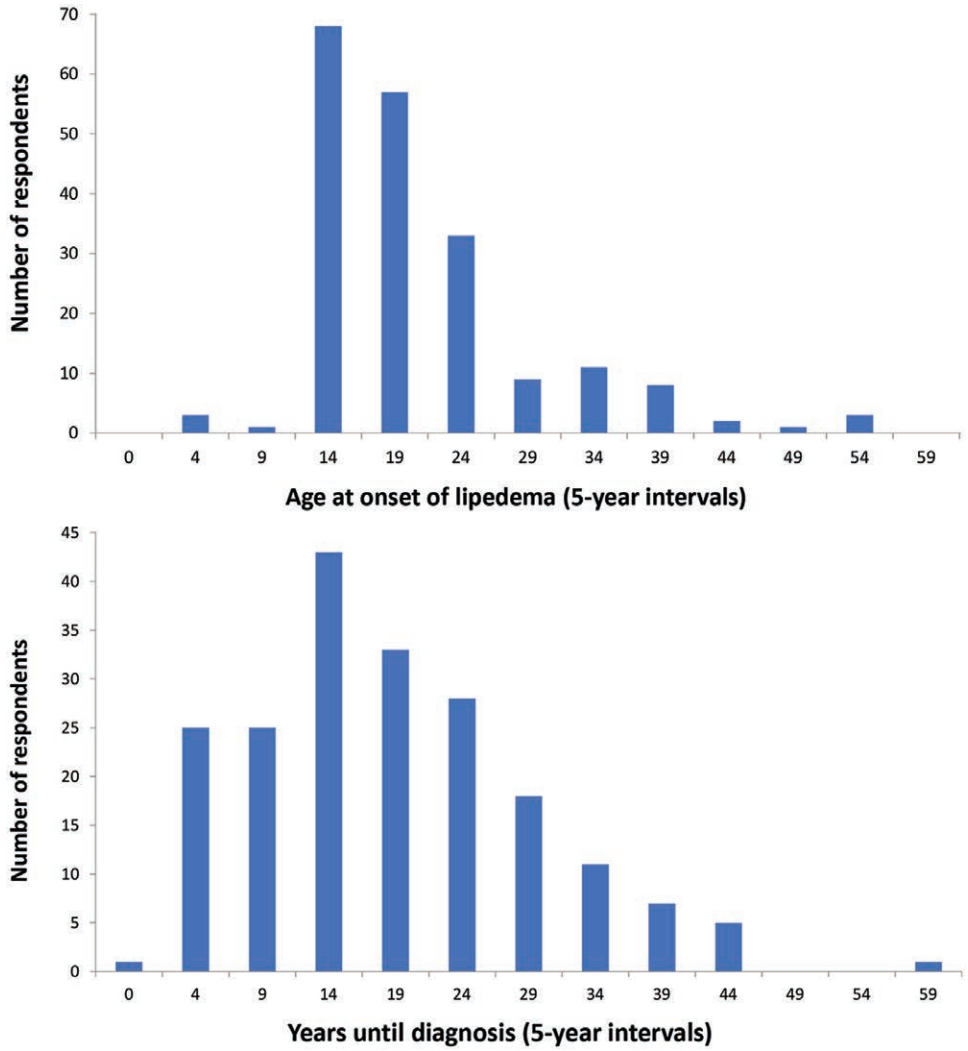

Fig. 1. (*Above*) Age at onset of lipedema. The mean age at which participants noticed lipedema symptoms for the first time was 16 years, with a standard deviation of 9 years. The most advanced age reported was 54 years. Each time point represents a 5-year interval. (*Below*) Years until diagnosis. The mean number of years before diagnosis was 15, with a standard deviation of 10. The shortest period until diagnosis was less than 1 year. Most of the respondents [n = 43 (20.6 percent)] reported having lived with the disease for 14 years, followed by 33 (15.8 percent) who reported 19 years. Each time point represents a 5-year interval.

pure fat removed from the patients was 10.1 liters, with a standard deviation of 9.6 liters. The average weight gain before surgery was 6.21 kg/year, with the highest total increase being 70 kg (n = 2) and the lowest increase being 2 kg (n = 39). Most patients gained 2 kg (n = 39), 4 kg (n = 36), and 6 kg (n = 36) per year. Following surgery, the patients' average weight was 84.3 kg.

Lipedema Inheritance

Most of the patients had relatives who were affected by lipedema. In most cases, grandmothers [74 (35.4 percent)] and mothers [62 (29.7 percent)] were affected, followed by aunts [48 (23.0 percent)], sisters [31 (14.8 percent)], and cousins [24 (11.5 percent)] (Fig. 3).

Lipedema Comorbidities

Our study revealed that some of the patients suffered from additional diseases besides lipedema. Hypothyroidism was the most frequently observed comorbidity, as indicated by 75 respondents (35.9 percent), followed by allergies [72 (34.4 percent)] and depression [48 (23.0 percent)]. Forty-seven (22.5 percent) suffered from a diagnosed migraine before surgery. Forty-five

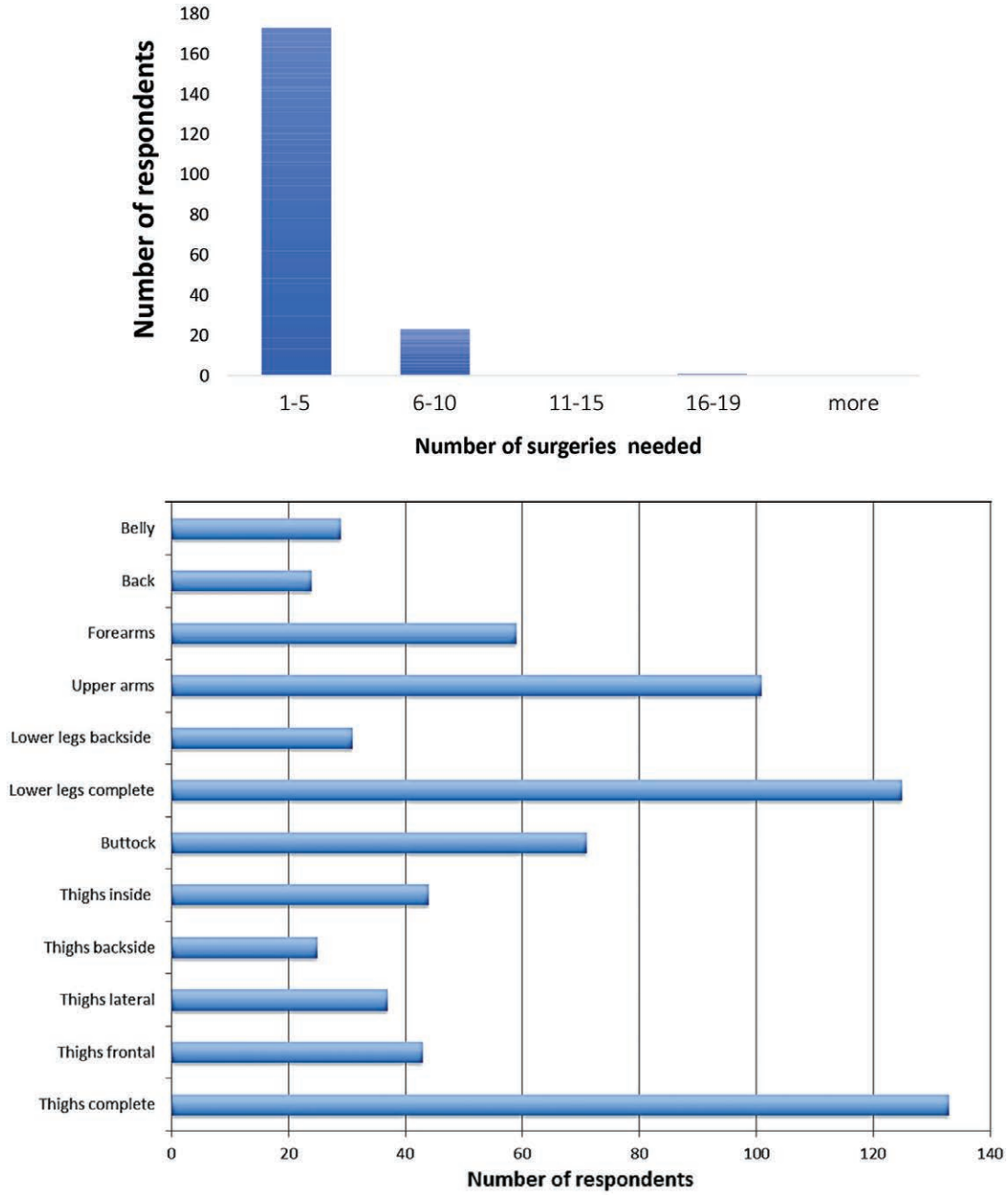

Fig. 2. (*Above*) Number of operations needed. The lowest number of operations conducted on lipedema patients was one and the highest was 16. The average number of operations ± SD conducted was 3 ± 2. (*Below*) Areas of liposuction.

patients (21.5 percent) suffered sleep disorders, 28 (13.4 percent) reported arterial hypertension, and 27 (12.9 percent) had asthma and bowel disorders. Other diseases mentioned by the respondents were rheumatism [n = 7 (3.3 percent)], diabetes type 1 [n = 3 (1.4 percent)], diabetes type 2 [n = 2 (1 percent)], polycystic ovary syndrome [n = 12 (5.7 percent)], and a high level of cholesterol (dyslipidemia) [n = 15 (7.2 percent)]. However, 43 respondents (20.6 percent) indicated not to have suffered from any of the above-mentioned diseases (Fig. 4).

Migraine

Among the 47 patients (23.7 percent) who suffered from a diagnosed migraine before surgery, 41 patients experienced at least five migraine attacks per month. The rest reported having experienced at least 10 migraine attacks per month. Following liposuction, the majority of the migraine patients

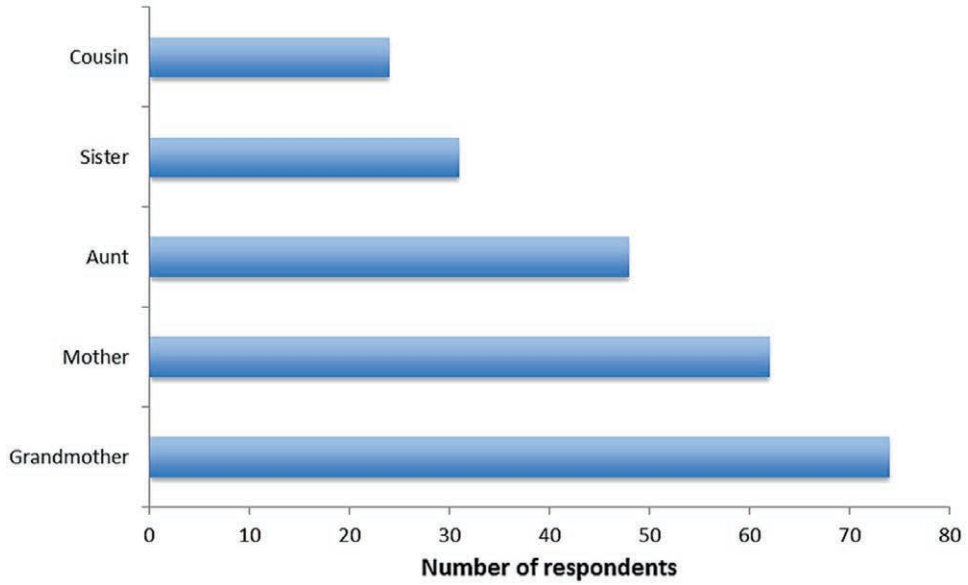

Fig. 3. Relatives affected by lipedema. In most cases, grandmothers [74 (35.4 percent)] and mothers [62 (29.7 percent)] were affected, followed by aunts [48 (23.0 percent)], sisters [31 (14.8 percent)], and cousins [24 (11.5 percent)].

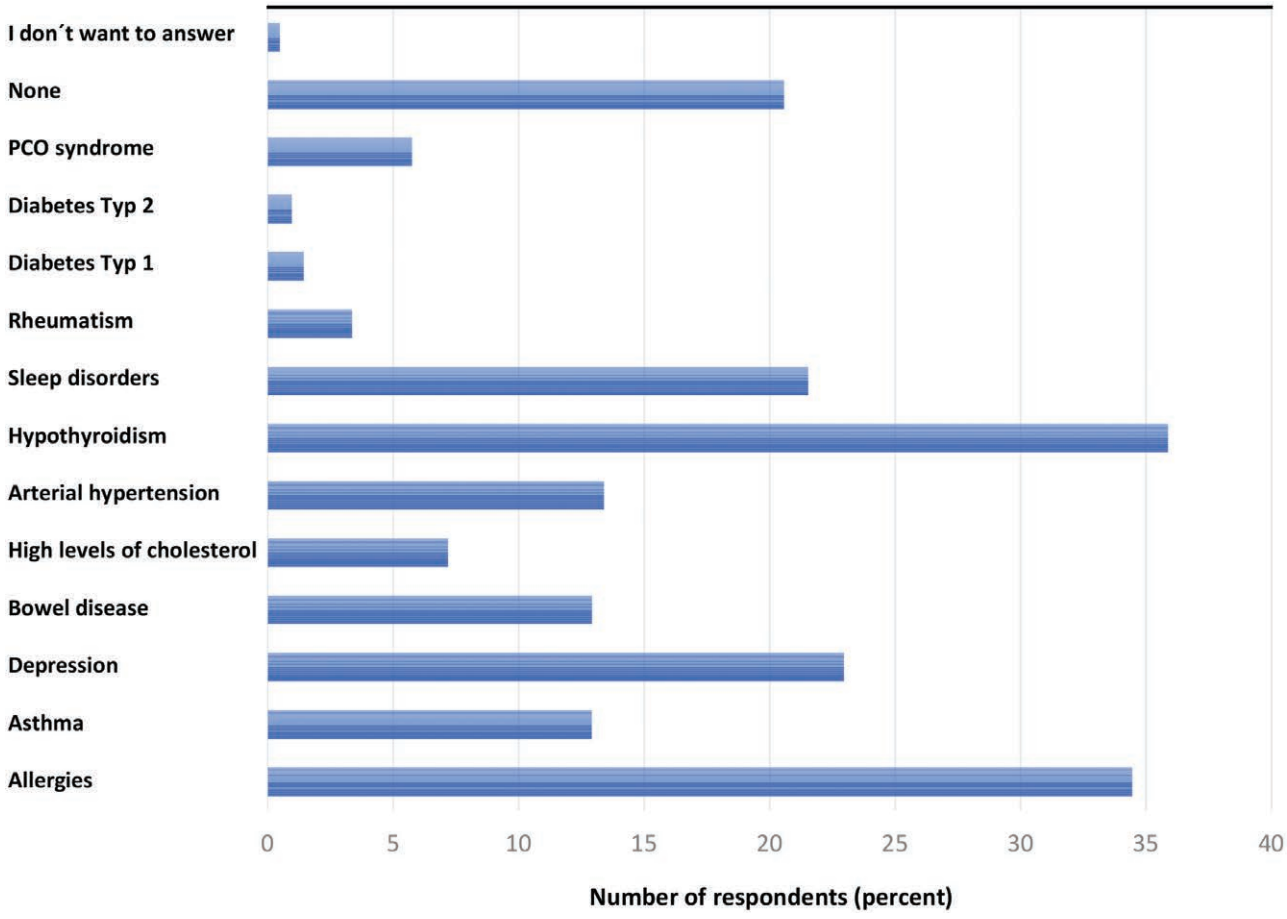

Fig. 4. Comorbidities among lipedema patients.

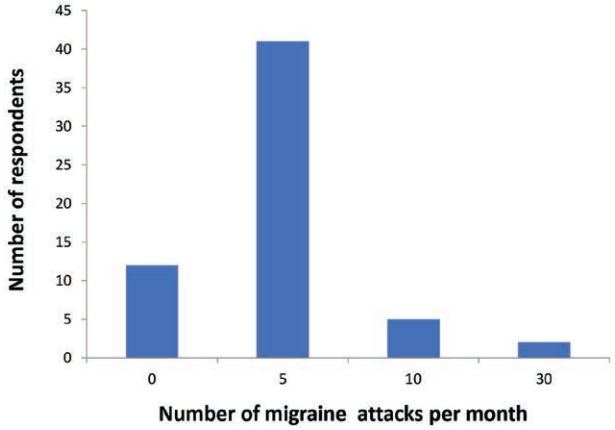

Fig. 5. Number of migraine attacks before liposuction. Among the 47 patients who suffered from a diagnosed migraine before surgery, 41 patients experienced migraine attacks at least five times per month. The rest reported having experienced migraine attacks at least 10 times per month.

[$n = 19$ (40.4 percent)] reported only one migraine attack per month (Figs. 5 and 6). In addition, 14 (29.8 percent) pointed out that the intensity of the migraine attacks had subsided after their surgery, 25 (53.2 percent) stated that the frequency of migraine attacks had declined, 10 (21.3 percent) did not experience migraine attacks any longer, and 15 (31.9 percent) did not observe any significant improvement following liposuction (Fig. 7).

Lipedema-Associated Pain

Subsequently, our study sought to examine the pain condition of lipedema patients. More than three-quarters ($n = 169$) of the respondents mentioned severe preoperative pain, whereas 19 (10 percent) were affected by only mild pain. Following liposuction, 164 of the respondents (97.0 percent) pointed out that the pain had diminished significantly after the operation (Fig. 8, *above*). Concomitantly, tenderness and pressure pain decreased significantly following liposuction. Improvements of 50 percent, 75 percent, and 100 percent have been reported by the majority of patients (Fig. 8, *below*, *left*). One hundred ninety-one of the respondents (91.4 percent) stated that they often suffered bruises and hematoma, a phenomenon that improved after the operation, as attested to by 147 of the participants (77.0 percent) (Fig. 8, *below*, *right*).

Lipedema-Associated Imbalances of Sexual Hormones

The study further revealed that 51 (30.5 percent) of the premenopausal respondents ($n = 167$) suffered imbalances of sexual hormones, whereas 116 (69.5 percent) did not. Of the 51 patients who suffered imbalances of sexual hormones, 20 (39.2 percent) recovered following liposuction, whereas the rest did not (Fig. 9).

Lymphatic Drainage and Patient Satisfaction

Because of the reduced swelling following liposuction, the necessity for lymphatic drainage has decreased substantially among lipedema patients. Before liposuction, a majority of the respondents received lymphatic drainage one (65 patients) or two times (89 patients) per week, followed by 12 individuals who received drainage three times per week. Only four patients received lymphatic drainage more often. The number of patients who received lymphatic drainage within

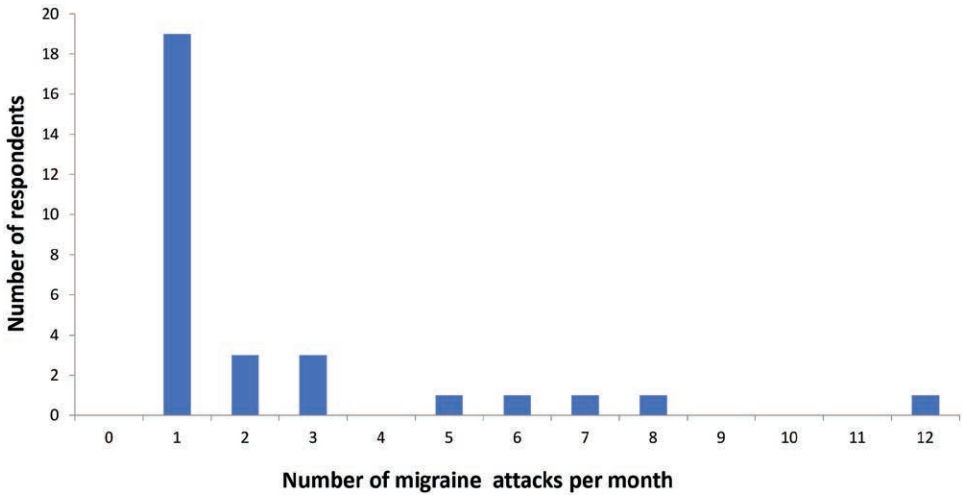

Fig. 6. Number of migraine attacks after liposuction; 19 of the migraine patients (40.4 percent) reported only one migraine attack per month.

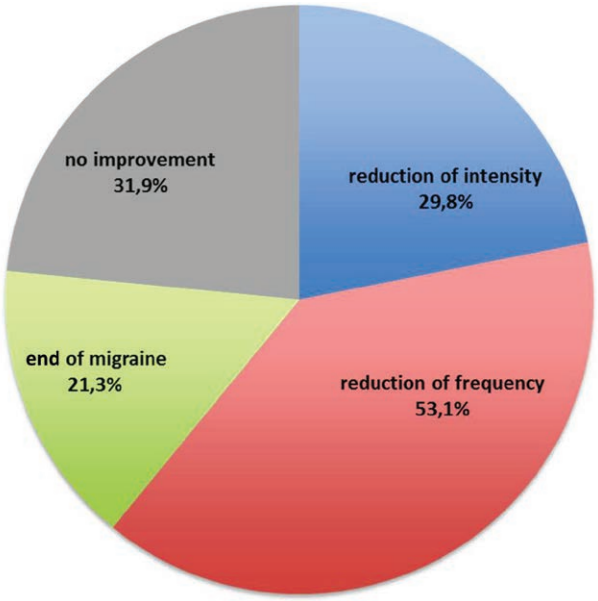

Fig. 7. Improvement of migraine after liposuction. Fourteen of the respondents (29.8 percent) reported that the intensity of the migraine attacks had subsided, 25 (53.2 percent) stated that the frequency of migraine attacks had declined, 10 (21.3 percent) did not experience migraine attacks any longer, and 15 (31.9 percent) did not observe any improvement.

3 to 6 months after their operations was significantly reduced. Seventy-eight patients had not received lymphatic drainage during that period, 42 received it once, and 67 received it twice, and 11 had lymphatic drainage at least three times within the same period after surgery. Before liposuction, 163 respondents (78 percent) wore compression garments for up to 24 hours/day, and 20 patients (9.6 percent) could not wear the garments because of pain. After surgery, slightly more than half of the patients indicated not having worn the compression garment any longer, whereas 49.3 percent still did. Ninety-eight percent of the respondents stated that they would undergo surgery again and recommend it to their affected relatives and friends.

DISCUSSION

Frequently, lipedema patients go through a long period of uncertainty and self-doubt before their disease is finally properly diagnosed. They are helpless against their weight gain, their pain, and also the social withdrawal they often experience. The majority of the respondents participating in our survey experienced first symptoms mostly during puberty up to the beginning of the third decade, which is in accordance with earlier reports.[8] Our data further confirm that there is a hereditary component to lipedema, as already described in the literature.[6] There is a general agreement that liposuction yields long-lasting positive effects in lipedema patients, leading to a marked increase in their quality of life.[10–12] This is further confirmed by our results.

In our survey, we focused not only on the overall postoperative improvement of clinical and physical parameters but also on comorbidities, which might be directly or indirectly related to lipedema. In the following, only those comorbidities whose frequencies were above average epidemiologic values are discussed further. For instance, although a relatively high percentage of respondents stated they suffered from allergies, it did not exceed the average prevalence of allergic diseases in Germany.[13,14]

Our study shows that hypothyroidism is one of the most frequent diseases found among lipedema patients. A prevalence of 35 percent is far beyond average, according to a screening of large population samples from the United States and Europe.[15] Data from the literature suggest that the occurrence of hypothyroidism varies substantially among lipedema patient cohorts.[16,17] Furthermore, there is evidence that hypothyroidism correlates with a higher body mass index and a higher prevalence of obesity, although the interplay between obesity and hypothyroidism is not yet clear.[18] It remains to be clarified whether hypothyroidism in lipedema patients is primarily associated with a body mass index greater than 26 kg/m^2, which is often found among lipedema patients.

According to our results, migraine tends to occur with increased frequency in lipedema patients. Interestingly, after liposuction, the majority of the respondents affected reported a reduced frequency and/or intensity of migraine attacks. Even the complete disappearance of migraine attacks has been observed. The connection between liposuction and the reduction of migraine attacks is not yet clear. Because migraine may be triggered by various nonspecific stimuli such as stress and depression, which are often observed in lipedema patients, it is conceivable that this vicious cycle is interrupted by the liposuction and the subsequent weight loss.

The prevalence of depression was high among lipedema patients, as stated by 23 percent of the respondents. This is clearly beyond the normal prevalence of depressive symptoms and diagnosed depression among adults in Germany.[19] Similar observations were made in a study on the prevalence of depression in obese patients, and

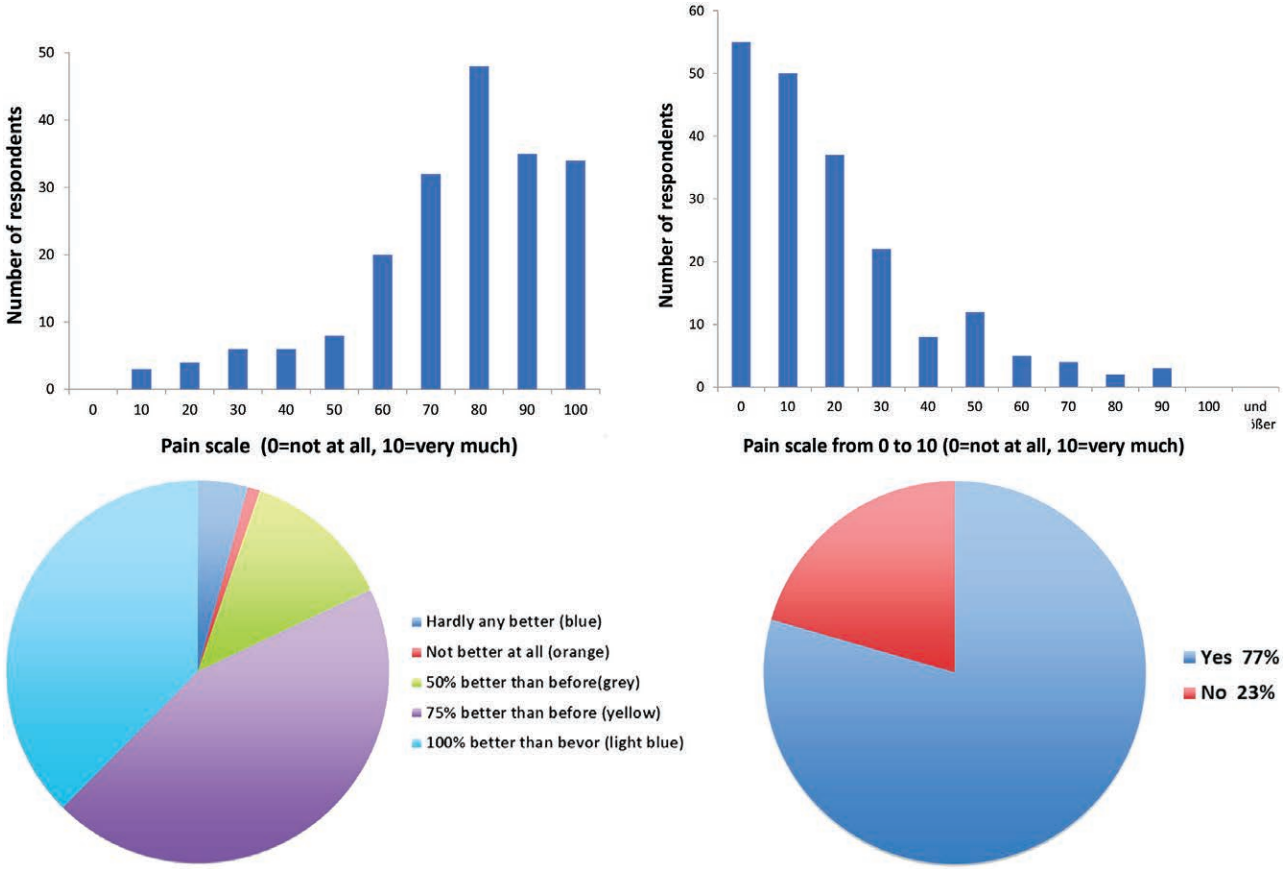

Fig. 8. (*Above*, *left*) Pain condition before liposuction. More than three-quarters (*n* = 169) of the respondents mentioned severe pain, whereas 19 (10 percent) were affected by mild pain. (*Above*, *right*) Pain condition after liposuction. One hundred sixty-four of the respondents (97.0 percent) pointed out that the pain had diminished significantly. (*Below*, *left*) Improvement of tenderness and pressure pain after liposuction. Improvements of 50 percent (*n* = 24), 75 percent (*n* = 24), and 100 percent (*n* = 71) were reported by the majority of patients. A slight improvement was reported by eight respondents, whereas only two patients did not feel any reduction of tenderness and pain. (*Below*, *right*) Reduction of hematoma formation and bruising after liposuction. One hundred ninety-one of the respondents (91.4 percent) stated that they often suffered bruises and hematoma, a phenomenon that improved after surgery, as attested to by 147 of the participants (77.0 percent) (Fig. 7, *below*).

a strong correlation between obesity and depression was found.[20] Because depressive symptoms were significantly reduced following liposuction, it may be speculated that the depressive mood was basically elicited by a combination of overweight and pain, reinforced by sleep disorders.

Pain and skin hypersensitivity to palpation are major characteristics distinguishing lipedema from lifestyle-induced obesity. This is also confirmed by our results showing that more than three-quarters of the respondents suffered severe pain before liposuction, a condition that ameliorated markedly after surgery. The physiologic mechanisms underlying lipedema-associated pain are still unclear, and convincing experimental data explaining this phenomenon are still missing. The current knowledge of lipedema-related pain has been summarized in a comprehensive review published recently.[21]

Interestingly, diabetes types 1 and 2 were particularly underrepresented among lipedema patients, which is another important feature distinguishing lipedema from obesity.[22,23] Moreover, our data show that the frequency of arterial hypertension among lipedema patients was below the average prevalence of the German population. This is in contrast to obesity-associated comorbidities, where the prevalence of arterial hypertension was found to correlate with a significant increase in the prevalence of obesity.[24] Furthermore, our data have shown that cholesterol levels were not increased in lipedema patients. On the contrary, obesity-related dyslipidemia has been well described.[25,26] In summary, no relation of lipedema to diabetes, hypertension, or dyslipidemia could be observed, which supports earlier reports.[27]

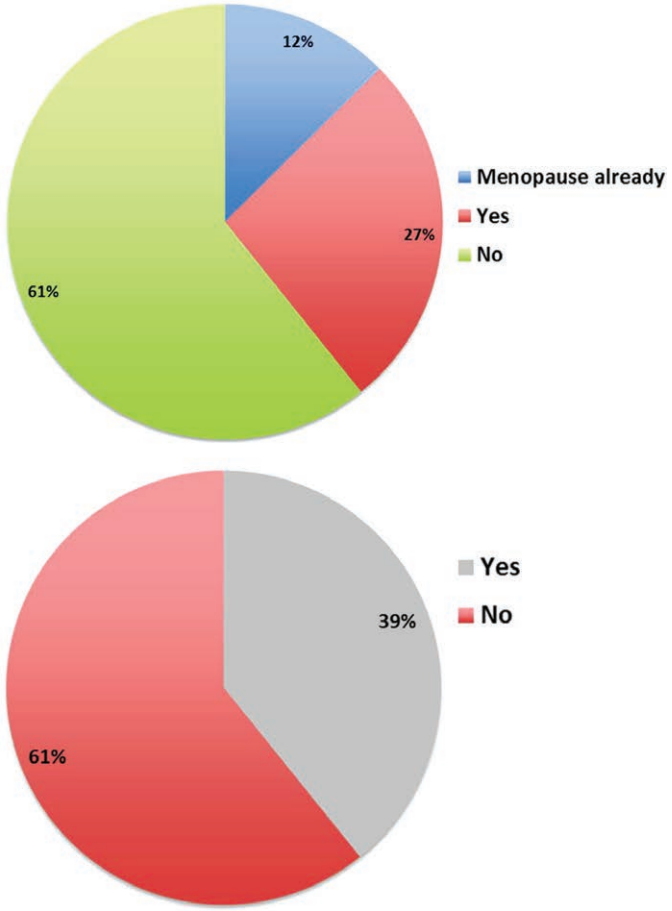

Fig. 9. (*Above*) Number of patients suffering imbalances of sexual hormones before liposuction. Fifty-one (30.5 percent) of the premenopausal respondents (n = 167) suffered imbalances of sexual hormones, whereas 116 (69.5 percent) did not. (*Below*) Improvement of imbalances of sexual hormones after liposuction. Of the 51 patients who suffered imbalances of sexual hormones, 20 (39.2 percent) recovered following liposuction, whereas the rest did not.

Another comorbidity questioned was polycystic ovary syndrome, a complex gynecologic disease that can cause infertility. Because polycystic ovary syndrome is sometimes referred to as the "metabolic syndrome of the ovaries," interest was high concerning a potential co-prevalence with lipedema. Considering the prevalence of polycystic ovary syndrome in Europe (4 to 12 percent), our data do not provide evidence to suggest that lipedema is associated with polycystic ovary syndrome.

A limitation of our findings might be the online study type and the low level of evidence. In addition, recall bias cannot be excluded because patients had to remember symptoms they had probably long before the operation and also might have been confused when symptoms overlapped. Because of the type of study design, self-reporting bias has to be considered.

CONCLUSIONS

Results from our survey indicate that lipedema, in contrast to obesity, is not linked to metabolic diseases, including diabetes type 1 or 2, arterial hypertension, or dyslipidemia. However, depression and hypothyroidism among lipedema patients were found to exceed the average prevalence in the German population. Thus, it will be of particular interest to find out whether there is any causal relationship between hypothyroidism and lipedema in further studies. Our data further confirm that the surgical treatment of lipedema ameliorates the patients' conditions in many aspects. Following liposuction, quality of life increases

significantly, with a reduction of pain, swelling, and bruising. Interestingly, a reduction and amelioration of a preexisting migraine in lipedema patients could be observed. Although the onset of lipedema has often been shown to coincide with major hormonal changes in women, a clear picture of the physiologic mechanisms underlying this progressive disease cannot be fully drawn without further granular cohort studies.

Anna-Theresa Bauer, M.D.
Klinikum rechts der Isar
Technischen Universitat Munchen
Plastische Chirurgie
Ismaningerstr 22
Muenchen 81675, Germany
anna-theresa.bauer@mri.tum

ACKNOWLEDGMENT

The authors gratefully acknowledge R. Kraus for lipedema patient acquisition and coordination.

REFERENCES

1. Halk AB, Damstra RJ. First Dutch guidelines on lipedema using the international classification of functioning, disability and health. *Phlebology* 2017;32:152–159.
2. Forner-Cordero I, Szolnoky G, Forner-Cordero A, Kemény L. Lipedema: An overview of its clinical manifestations, diagnosis and treatment of the disproportional fatty deposition syndrome: Systematic review. *Clin Obes.* 2012;2:86–95.
3. Wenczl E, Daróczy J. Lipedema, a barely known disease: Diagnosis, associated diseases and therapy (in Hungarian). *Orv Hetil.* 2008;149:2121–2127.
4. Reich-Schupke S, Schmeller W, Brauer WJ, et al. S1 guidelines: Lipedema. *J Dtsch Dermatol Ges.* 2017;15:758–767.
5. Fife CE, Maus EA, Carter MJ. Lipedema: A frequently misdiagnosed and misunderstood fatty deposition syndrome. *Adv Skin Wound Care* 2010;23:81–92; quiz 93–94.
6. Child AH, Gordon KD, Sharpe P, et al. Lipedema: An inherited condition. *Am J Med Genet A* 2010;152:970–976.
7. Buck DW II, Herbst KL. Lipedema: A relatively common disease with extremely common misconceptions. *Plast Reconstr Surg Glob Open* 2016;4:e1043.
8. Warren Peled A, Kappos EA. Lipedema: Diagnostic and management challenges. *Int J Womens Health* 2016;8:389–395.
9. Földi M. Lipedema. In: Földi M, Földi E, eds. *Földi's Textbook of Lymphology: for Physicians and Lymphedema Therapists.* 3rd ed. Munich, Germany: Elsevier; 2006:417–427.
10. Baumgartner A, Hueppe M, Schmeller W. Long-term benefit of liposuction in patients with lipoedema: A follow-up study after an average of 4 and 8 years. *Br J Dermatol.* 2016;174:1061–1067.
11. Dadras M, Mallinger PJ, Corterier CC, Theodosiadi S, Ghods M. Liposuction in the treatment of lipedema: A longitudinal study. *Arch Plast Surg.* 2017;44:324–331.
12. Szolnoky G. Currently the best treatment for lipoedema. *Br J Dermatol.* 2016;174:959–960.
13. Langen U, Schmitz R, Steppuhn H. Prevalence of allergic diseases in Germany: Results of the German Health Interview and Examination Survey for Adults (DEGS1) (in German). *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz.* 2013;56:698–706.
14. Bergmann KC, Heinrich J, Niemann H. Current status of allergy prevalence in Germany: Position paper of the Environmental Medicine Commission of the Robert Koch Institute. *Allergo J Int.* 2016;25:6–10.
15. Vanderpump MP. The epidemiology of thyroid disease. *BMJ* 2011;99:39–51.
16. Herbst KL, Mirkovskaya L, Bharhagava A, Chava Y, Te CHT. Lipedema fat and signs and symptoms of illness, increase with advancing stage. *Arch Med.* 2015;7:1–8.
17. Schubert N, Viethen H. Lipödem und Liplymphödem: Alles eine Frage des Lebensstils? *Lymph Forsch.* 2016;20:18–27.
18. Sanyal D, Raychaudhuri M. Hypothyroidism and obesity: An intriguing link. *Indian J Endocrinol Metab.* 2016;20:554–557.
19. Busch MA, Maske UE, Ryl L, Schlack R, Hapke U. Prevalence of depressive symptoms and diagnosed depression among adults in Germany: Results of the German Health Interview and Examination Survey for Adults (DEGS1) (in German). *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz.* 2013;56:733–739.
20. Willage B. The effect of weight on mental health: New evidence using genetic IVs. *J Health Econ.* 2018;57:113–130.
21. Brenner E. What causes pain in lipedema. *Lymph Forsch.* 2017;21:2–9.
22. Al-Goblan AS, Al-Alfi MA, Khan MZ. Mechanism linking diabetes mellitus and obesity. *Diabetes Metab Syndr Obes.* 2014;7:587–591.
23. Bhupathiraju SN, Hu FB. Epidemiology of obesity and diabetes and their cardiovascular complications. *Circ Res.* 2016;118:1723–1735.
24. Praso S, Jusupovic F, Ramic E, et al. Obesity as a risk factor for arterial hypertension. *Mater Sociomed.* 2012;24:87–90.
25. Feingold KR, Grunfeld C. Obesity and dyslipidemia. In: De Groot LJ, Chrousos K, Dungan, Feingold KR, et al., eds. *Endotext.* South Dartmouth, Mass: MDText.com; 2000:332–342.
26. Klop B, Elte JW, Cabezas MC. Dyslipidemia in obesity: Mechanisms and potential targets. *Nutrients* 2013;5:1218–1240.
27. Torre YS, Wadeea R, Rosas V, Herbst KL. Lipedema: Friend and foe. *Horm Mol Biol Clin Investig.* 2018;33:1.