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Original Research Articles

Liposuction May Reduce Pain in Dercum's Disease (Adiposis Dolorosa)

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Abstract

Objective. The aim of this prospective study is to assess the effect of liposuction on the pain experienced by women with Dercum's disease (adiposis dolorosa).

Design. Pain was examined preoperatively and at 3 months, and 1, 2, 3, and 5 years after liposuction. The subjective pain sensation was evaluated with a visual analog scale and number of words chosen, and the objective pain sensation with the mechanical pressure pain threshold.

Setting. Dercum's disease is characterized by obesity and pronounced pain in the adipose tissue. The pain is chronic and often disabling and resistant to traditional analgesics and other pain treatment. However, five reports have been published on the encouraging effect of liposuction.

Patients. Pain was evaluated in 53 patients with Dercum's disease that had been operated on with liposuction. As controls, 58 nonoperated subjects with Dercum's disease and 41 obese abdominoplasty patients were followed for 5 years.

Results. Both subjective and objective pain measurements revealed a statistically significant decrease in the pain experienced by the Dercum patients after surgery as compared with preoperatively. However, the pain relief diminished over time. Furthermore, a significant postoperative difference could be seen between the Dercum operated group and the Dercum controls as regards measured pain. The difference decreased over time but still lingered 5 years postoperatively.

Conclusion. The results suggest that liposuction might alleviate pain in patients with Dercum's disease. However, it is difficult to determine whether the effect is due to the actual surgery or to other factors.

Key Words. Dercum's Disease; Liposuction; Pain Evaluation; Adiposis Dolorosa; Five-Year Follow-Up

Introduction

Dercum's disease (adiposis dolorosa) is characterized by pronounced pain in the adipose tissue and a number of associated symptoms. The diagnosis is based on clinical symptoms [1]. The pain is chronic (>3 months) and often disabling and resistant to analgesics such as paracetamol and dextroproxyphen [2,3]. Other proposed treatments, for instance lignocain infusions, often have insufficient or merely temporary effect [2,3]. However, five case reports [4–8] have been published on the encouraging effect of liposuction, showing that nine patients experienced a considerable subjective pain relief postoperatively with a follow-up between 1 and 2 years. None of the reported patients experienced any recurrence of pain within this time. To our knowledge, no long-term study concerning the effect of liposuction on patients with Dercum's disease has been performed on a larger population. The aim of this prospective study is to assess the long-term effects of liposuction on the pain experienced by women with Dercum's disease.

Patients and Methods

Patients and Controls

A total of 111 patients fulfilling the clinical criteria of Dercum's disease, that is obesity and chronic pain (>3 months) in the adipose tissue [9], were referred consecutively to our clinic by the same consultant. Diagnosis was based on the medical history evaluated from a standardized questionnaire and a systematic physical examination on three separate visits. All the patients had general

Table 1 Patients' profile. Mean (SD)

	Dercum Operated (N = 53)	Dercum Controls (N = 58)	Abdominoplasty Patients (N = 41)
Age (years)	52 (10)	51 (11)	49 (11)
Height (cm)	164 (9)	164 (7)	165 (5)
Weight (kg)	91 (16)	94 (19)	90 (15)
BMI (kg/m^2)	34 (6)	35 (7)	38 (6)

BMI = body mass index; SD = standard deviation.

diffuse disease, that is, they did not have any lipomas. Indication for operation was pain in the adipose tissue. All referred patients were enrolled in the study. The first 53 refered patients were consecutively operated on with liposuction. This group was entitled "Dercum operated." The following 58 women with Dercum's disease were recruited as controls. This group was called "Dercum controls." The patients were given no restriction in traditional pain medication and no particular advice regarding lifestyle. No other treatment, such as lignocaine infusions or steroids, was commenced during the course of the study. In addition, 41 women, with no acute or chronic pain, that were to be operated on with abdominoplasty, were recruited as controls. This group was named "Abdominoplasty patients." The patient's profile is shown in Table 1. There were no statistical differences between the groups as regards to age or body mass index (BMI).

Methods

Surgical Technique

Liposuction was performed under general anesthesia, epidural or spinal block. Neither local anesthetic nor epinephrine was injected locally, hence the "dry technique" was used. Painful areas such as the abdomen, flanks/hips and gluteal regions, proximal thighs/legs and arms and the medial areas of the knees were operated on. Four-millimeter incisions were made and a bullet-shaped cannula, with two or three openings distally and an outer diameter of 5–6 mm, was used. A vacuum pump connected to the cannula gave rise to a negative atmospheric pressure of 0.9. All operations were performed by one of the authors (HB). All patients received anticoagulants, the great majority in the form of dextran, during surgery. Following liposuction, the treated areas were firmly compressed, by means of compression garments on the legs, elastic bandages on the arms, and an elastic corset on the torso, to achieve hemostasis and to prevent postoperative edema in the operated areas. Compression was maintained for at least 6 weeks. No symptomatic postoperative deep venous thrombosis was seen.

The aspirate was collected in 2,000 mL plastic containers graded to an accuracy of 20 mL. The aspirate was homogenized by vigorous shaking, and 2–3 samples of 50 mL each were centrifugated for 20 minutes at 3,000 rpm. Following centrifugation, the percentage of adipose tissue in the aspirate was measured. The fat weight was calculated using the known density of fat (0.9167 g/mL ≈ 0.92 g/cm^3) [10]. Ten of the patients were also subjected to abdominoplasty. The weight of the excised fat was added to the weight of the fat in the aspirate, thus giving the total weight of removed fat.

Weight and BMI

The patients' body weight was measured on the same scales. The weight was registered with an accuracy of 0.1 kg. BMI values were calculated as the ratio of the body mass in kilograms and the square of height in meters.

Subjective Pain Measurements

To evaluate the patients' subjective pain sensation a modified version of the Pain-O-Meter was used [11]. The method consists of a questionnaire comprising a visual analog scale (VAS) and number of words chosen (NWC). In combination, the two tools evaluate both the quality and the intensity of the pain sensation, as validated by Gaston-Johansson [11]. In addition, the operated patients were asked to indicate, ticking "yes" or "no" in a questionnaire, whether they thought that the liposuction had diminished their pain or not. All patients received careful instructions on how the VAS and NWC questionnaires should be filled out. The subjective pain sensation was only evaluated in the subjects with Dercum's disease. The questionnaires regarding VAS, NWC, and whether surgery had reduced their pain or not, when applicable, were answered preoperatively and after 3 months, and 1, 2, 3, and 5 years postoperatively.

VAS is widely used as an easy, reliable, and sensitive means with which to evaluate patients' subjective evaluation of the outcome of various treatments in clinical studies, particularly on pain [12]. The scale used was a straight line (10 cm) on which the patient made a mark corresponding to her appraisal of pain [12].

The NWC questionnaire comprises a list of 12 sensory and 11 affective pain descriptors in a random order. NWC aims to evaluate the sensory and affective dimension of the pain experienced. The patients were shown a list of the words and asked to select and mark the words that described their pain. Each descriptor was then assigned a weighed value (range 1–5), giving a total pain intensity score, one for the sensory component of pain and one for the affective component. The weighed value is associated with the following words: 1 = mild, 2 = discomforting, 3 = distressing, 4 = horrible, and 5 = excruciating [13]. The patients could choose as many words as needed to describe their pain. The words used were based on Gaston-Johansson's validity and reliability research [11] on a translated, shortened, and modified version of the McGill Pain Questionnaire [13]. The Swedish short-form McGill Pain Questionnaire has been validated among different patient groups [14].

Objective Pain Measurements

During the initial course of the study, a device, an analog algometer, was constructed by the Department of Biomedical Engineering in our hospital. The algometer aimed at measuring the mechanical pressure pain threshold (PPT) in N/cm^2. The PPT was determined in the last 28 Dercum patients that were operated on and in all women in the two control groups.

The PPT was measured on the right and the left side of the abdomen and on the knees bilaterally. In order to locate the measure points at follow-up, photos were taken of the subjects with the measuring points marked, indicating distances (cm) to well-known fixed anatomical landmarks. Measurements were performed on folds containing skin and adipose tissue, thus underlying muscle tissue was not involved. The patients were instructed to press a button, giving a light indication to the investigator, when the pain became unbearable. The readout on the algometer was locked and then noted. Care was taken to always use the same rate of pressure application. The diameter of the probe was 14 mm. The same investigator performed all measurements. Three measurements where obtained on each measuring point, and the mean was calculated and used as the observation value. The same procedure was done preoperatively and then repeated after 3 months, and after 1, 2, 3, and 5 years.

Validation of the Algometer

The algometer was repeatedly tested with known weights during the trial and showed no drift. To evaluate the test–retest reliability, three measuring procedures were performed by one investigator on three consecutive days in 27 Dercum patients. Mean differences of the pressure with 95% limits of agreements (prediction limits for differences between individual measurements) and 95% confidence interval to the limits of agreement were calculated between days (1, 2, and 3) for four different locations (abdomen left, abdomen right, knee left, and knee right). Bland–Altman plots were made to estimate whether difference and variance was constant across the range of measurements (Figure 1) [15].

Statistical Methods

Wilcoxon signed-ranks test was used to assess the difference between values preoperatively and at the different follow-up times within the groups. Mixed model analyses were used to test the difference between the groups. The residuals were normally distributed. The mixed models were performed on the repeated measures of the difference of pain scores from baseline as dependent variables; group, follow-up time, and their interaction as fixed factors, and subject as random factor. The mixed model analyses included age, BMI, and each dependent variable's preoperative value as covariates. AR [1] was chosen as covariance structure. The statistical tests were performed in SPSS 15.0 for Windows (SPSS Inc., Chicago, IL). We regarded a $P < 0.05$ as indicating a statistically significant difference.

Ethics

The study was approved by the Ethics of Human Investigation Committee at Lund University, LU 236–89 and LU 422–91. All participants gave their informed consent to participate. The procedures followed were in accordance with the Helsinki Declaration of 1964, as revised.

Results

The weight and BMI of the subjects during the trial are shown in Table 2. The average amount of fat removed in the Dercum operated group was 3,749 ± 2,325 g (mean ± standard deviation [SD], range: 580–10,430 g).

Validation of the Algometer

An overall assessment of the comparisons between days of pressure measurements shows that the directions of the mean differences vary between the locations but seem fairly close to zero. The limits of agreements of the differences were generally within the range of –10–10 N/cm^2, which is considered to show acceptable accordance (Table 3). The 95% confidence intervals for the limits of agreement of the data measured on consecutive days by the investigator confirm an acceptable accordance. Figure 1 shows a Bland–Altman plot of the measurements.

Pain Measurements

Results are shown in Tables 4–9 and Figures 2–6. In brief, both subjective and objective pain measurements revealed reduced pain experienced by the Dercum patients postoperatively compared with preoperatively. However, the improvement faded over time. Nonetheless, it was still statistically significant 5 years postoperatively, as measured with VAS (Tables 4 and 5, Figure 2), NWC (Tables 6 and 7, Figure 3), and PPT (Tables 8 and 9, Figures 4 and 5). The number of patients who thought the operation had decreased their pain was 80% 3 months postoperatively but had decreased to 45% after 5 years (Figure 6).

Postoperatively, a statistically significant difference could be seen between the Dercum operated group and the Dercum controls. The difference diminished over time but still lingered 5 years postoperatively.

Discussion

Material

The strength of the present study is that the diagnosis of Dercum's disease was made by the same consultant and that the same surgeon operated all the patients. An inherent weakness of any long-term clinical study is that there

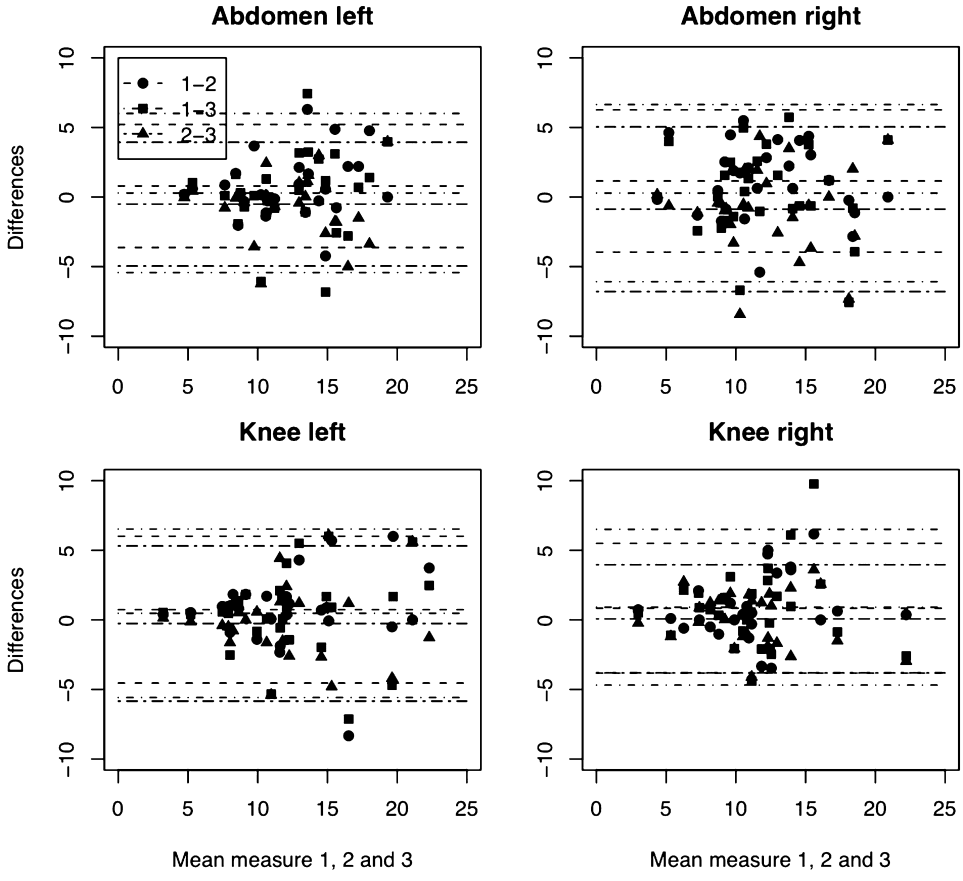

Figure 1 Bland–Altman plots of pressure measurements (N/cm^2) on three consecutive days made by investigator 1 are shown for the four different locations (abdomen left, abdomen right, knee left, and knee right). Measure differences between days (1–2, 1–3, and 2–3) vs the average of first, second, and third measurements are plotted. The middle lines represent the mean of differences. The other lines represent limits of agreements.

always are missing values. However, even though the follow-up in this study was 5 years, the majority of the patients were still included in the study when it was concluded. Missing vales were due to that patients did not come to the scheduled appointments. The PPT has been determined in a smaller number of the patients as this method was first introduced when the 26th subject was operated on.

Methods

Measuring pain is a difficult task due to the subjective character of this entity; nonetheless, we chose a number of different pain assessments to evaluate the effect of liposuction in Dercum's disease.

As regards VAS, Bigatti and Cronan [16] have shown that it has a high correlation with other pain measurements and a high correlation with symptoms in syndromes that encompass pain such as fibromyalgia. However, other studies have indicated that patients with greater pain require a greater change in VAS to experience a clinically significant pain relief [17].

As regards NWC, Perry et al. have concluded that it might be less valid for idiopathic chronic pain syndromes because this instrument is sensitive to psychological aspects and could give rise to a distorted perception of the pain [18]. On the other hand, Melzack has shown that changes in different psychological variables do not create variability in the word choices [13]. Furthermore, it has been suggested that NWC does not necessarily diminish with partial but not complete pain relief [13].

As regards the PPT measurements, the validation demonstrated that there is no inter-day difference in our measurements. This is in accordance with a study conducted by Nussbaum and Downes [19]. They concluded that PPT

Table 2 The patients' weight and BMI. Mean (SD)

	Dercum Operated (N = 53)	Dercum Controls (N = 58)	Abdominoplasty Patients (N = 41)
Weight (kg)			
Baseline	90.8 (16.0)	94.1 (18.9)	89.5 (15.1)
3 months	87.9 (12.1)	94.9 (19.9)	85.7 (18.9)
1 year	87.5 (18.6)	93.5 (19.7)	88.8 (14.6)
2 years	90.4 (15.2)	93.4 (17.3)	87.4 (14.4)
3 years	90.0 (14.7)	94.3 (17.0)	88.8 (15.6)
5 years	91.7 (16.5)	95.0 (18.1)	90.6 (16.3)
BMI (kg/m^2)			
Baseline	34.3 (5.7)	35.0 (6.8)	33.2 (5.5)
3 months	32.9 (4.2)	35.3 (7.0)	31.6 (6.6)
1 year	32.9 (6.7)	34.9 (7.0)	32.8 (5.0)
2 years	34.1 (5.2)	34.7 (6.0)	32.4 (4.6)
3 years	33.9 (4.9)	35.2 (5.8)	32.7 (5.0)
5 years	34.4 (5.6)	35.5 (6.3)	33.4 (5.3)

BMI = body mass index; SD = standard deviation.

measurements are reliable from day to day, particularly when performed by the same investigator, as in this case. There are several indicators that there may be an inter-investigator difference when PPT measurements are performed. In fact, we let a second investigator perform test measurements and a difference between the two investigators was seen. Furthermore, even though care was taken to always use the same rate of pressure application, our investigator was not timed, and therefore difference in rate applied and subsequent influence on the results cannot be excluded. Moreover, investigator expectancy and knowledge of measurements site characteristics could have caused measurement bias [20]. A strength of the present study is that all PPT measurements were performed by the same investigator.

Instrumental factors are also important. The PPT results are affected by the size of the probe, as the probe diameter determines in which tissue layer the PPT is measured. In fact, Takahashi et al. [21] have demonstrated that PPT measured with small probes (1.0 mm diameter) is affected by surface anesthetics, whereas large probes (1.6 and 15 mm diameters) are not. In other words, the skin nociceptors are suggested to play an insignificant role in the

Table 3 Mean differences between measurements on different days with limits of agreements

		Measure (N/cm^2)		
	N	1–2 Mean Difference (LoA*)	1–3 Mean Difference (LoA*)	2–3 Mean Difference (LoA*)
Observer				
Abdomen left	27	0.79 (–3.62 to 5.21)	0.29 (–5.43 to 6.01)	–0.51 (–4.95 to 3.94)
Abdomen right	27	1.16 (–3.95 to 6.27)	0.28 (–6.09 to 6.65)	–0.87 (–6.79 to 5.04)
Knee left	27	0.73 (–4.54 to 6.01)	0.47 (–5.58 to 6.52)	–0.26 (–5.84 to 5.32)
Knee right	27	0.84 (–3.82 to 5.50)	0.91 (–4.69 to 6.50)	0.073 (–3.81 to 3.96)

* 95% limits of agreement (LoA).

Table 4 Visual analog scale (VAS) between groups

					Difference in Change Over Time*	
	Dercum Operated		Dercum Control		Dercum Operated vs Dercum Control	
	N	Mean (SD)	N	Mean (SD)	Mean (95% CI)	*P* Value
VAS						
Baseline	53	6.4 (2.2)	41	5.9 (2.3)	Reference	
3 months	53	3.4 (2.8)	36	6.2 (2.2)	–3.3 (–4.4 to –2.2)	<0.001
1 year	52	4.4 (2.8)	30	5.2 (2.3)	–1.1 (–2.2 to 0.11)	0.074
2 years	51	4.7 (2.6)	30	5.4 (3.0)	–0.92 (–2.1 to 0.25)	0.124
3 years	47	4.7 (3.1)	23	6.5 (2.4)	–1.7 (–3.0 to –0.47)	0.007
5 years	43	4.9 (3.2)	25	6.1 (3.0)	–1.4 (–2.7 to –0.15)	0.028

* Mixed model analysis adjusting for age, BMI, and baseline VAS. Missing data that reduced the number of observations (n) in each test are shown in the table.
SD = standard deviation; CI = confidence interval.

Table 5 Visual analog scale (VAS) within groups

	n[1]	*P* Value
Dercum operated (N = 53)		
Baseline vs 3 months	53	<0.001
Baseline vs 1 year	52	<0.001
Baseline vs 2 years	51	0.000354
Baseline vs 3 years	47	0.00372
Baseline vs 5 years	43	0.000337
Dercum control (N = 58)		
Baseline vs 3 months	36	0.205
Baseline vs 1 year	30	0.106
Baseline vs 2 years	30	0.282
Baseline vs 3 years	23	0.771
Baseline vs 5 years	25	0.806

n[1] = matched pairs (Wilcoxon signed ranks). Each patient served as her own control. Missing data that reduced the number of paired observations (n) in each test are shown in the table.

total pain measured when larger probes are used, as they probably measure the pain experienced in deeper tissues. Our probe had a diameter of 14 mm. Moreover, the pressure transmission is influenced by tissue properties such as thickness [21]. Therefore, we believe that in the investigated patients, with pronounced obesity, mainly adipose nociception was measured and not that of the skin.

Results

Postoperative sensory change after liposuction is a well-known side effect. Different mechanisms have been suggested for the local sensitivity loss, even though the main theory concerns direct nerve trauma caused by the cannula. However, in a previous study, we have demonstrated that thermal and vibratory thresholds do not differ after liposuction in patients with Dercum's disease [22]. It is unlikely that direct nerve destruction alone explain the pain reduction seen in our patients following liposuction. Furthermore, the reduction in pain in Dercum's disease persisted longer than the sensibility loss normally persists after liposuction in healthy patients.

Both peripheral and central nervous etiologies have been proposed for the pain in Dercum's disease [23]. Our findings suggest that peripheral mechanism might play a major role. Specifically, the white adipose tissue is innervated by the sympathetic nervous system [24]. Dalziel [24]

Table 6 Total number of words chosen (NWC) between groups

					Difference in Change Over Time*	
	Dercum Operated		Dercum Control		Dercum Operated vs Dercum Control	
	N	Mean (SD)	N	Mean (SD)	Mean (95% CI)	*P* Value
Total						
Baseline	53	38.0 (13.3)	46	31.5 (15.6)	Reference	
3 months	53	19.3 (16.1)	40	28.6 (15.3)	−14.5 (−20.7 to −8.4)	<0.001
1 year	51	23.3 (17.6)	33	29.6 (19.1)	−9.7 (−16.1 to −3.4)	0.003
2 year	49	26.1 (19.5)	37	29.0 (17.2)	−6.5 (−12.8 to −0.18)	0.044
3 year	46	25.4 (19.3)	29	37.9 (20.2)	−13.9 (−20.5 to −7.3)	<0.001
5 year	44	23.8 (17.5)	31	30.7 (19.7)	−8.8 (−15.3 to −2.2)	0.009
Sensitive						
Baseline	53	19.6 (8.1)	46	16.4 (8.4)	Reference	
3 months	53	10.5 (8.8)	40	15.0 (8.2)	−6.9 (−10.3 to −3.5)	<0.001
1 year	51	12.2 (9.5)	33	16.0 (10.1)	−5.1 (−8.6 to −1.6)	0.005
2 year	49	13.9 (10.5)	37	15.0 (8.7)	−2.5 (−6.0 to 0.95)	0.154
3 year	46	13.1 (10.2)	29	19.6 (10.3)	−7.1 (−10.7 to −3.4)	<0.001
5 year	44	12.4 (9.6)	31	15.8 (10.1)	−4.2 (−7.9 to −0.57)	0.024
Affective						
Baseline	53	18.3 (7.5)	46	15.2 (8.3)	Reference	
3 months	53	8.8 (8.2)	40	13.6 (8.1)	−7.1 (−10.4 to −3.8)	<0.001
1 year	51	11.1 (8.9)	33	13.6 (9.7)	−4.2 (−7.6 to −0.77)	0.017
2 year	49	12.2 (9.5)	37	14.0 (9.4)	−3.5 (−6.9 to −0.12)	0.042
3 year	46	12.3 (9.7)	29	18.3 (10.8)	−6.4 (−9.9 to −2.9)	<0.001
5 year	44	12.1 (9.3)	31	14.9 (10.5)	−3.4 (−6.9 to 0.072)	0.055

* Mixed model analysis adjusting for age, BMI and baseline NWC. Missing data that reduced the number of observations (n) in each test are shown in the Table.
SD = standard deviation; CI = confidence interval.

Table 7 Number of words chosen (NWC) within groups

	n[1]	*P* Value (Total)	*P* Value (Sensitive)	*P* Value (Affective)
Dercum operated (N = 53)				
Baseline vs 3 months	53	<0.001	<0.001	<0.001
Baseline vs 1 year	51	<0.001	<0.001	<0.001
Baseline vs 2 years	49	<0.001	0.000864	<0.001
Baseline vs 3 years	46	<0.001	<0.000219	<0.001
Baseline vs 5 years	44	<0.001	<0.001	<0.001
Dercum control (N = 58)				
Baseline vs 3 months	40	0.149	0.251	0.106
Baseline vs 1 year	33	0.168	0.286	0.130
Baseline vs 2 years	37	0.0794	0.0523	0.281
Baseline vs 3 years	29	0.351	0.296	0.559
Baseline vs 5 years	31	0.426	0.260	0.520

n[1] = matched pairs (Wilcoxon signed ranks). Each patient served as his or her own control. Missing data that reduced the number of paired observations (n) in each test are shown in the table.

Table 9 Pain pressure threshold (PPT) within groups. Knee and abdomen

	Knee		Abdomen	
	n[1]	*P* Value	n[1]	*P* Value
Dercum operated				
Baseline vs 3 months	28	<0.001	27	<0.001
Baseline vs 1 year	28	<0.001	27	<0.001
Baseline vs 2 years	27	<0.001	26	<0.001
Baseline vs 3 years	28	<0.001	27	<0.001
Baseline vs 5 years	28	<0.001	27	<0.001
Abdominoplasty patients				
Baseline vs 3 months	40	0.824	40	0.602
Baseline vs 1 year	38	0.359	38	0.000870
Baseline vs 2 years	38	0.0193	38	<0.001
Baseline vs 3 years	37	0.00265	37	<0.001
Baseline vs 5 years	36	0.0492	36	<0.001
Dercum control				
Baseline vs 3 months	58	0.411	58	0.624
Baseline vs 1 year	58	0.843	58	0.680
Baseline vs 2 years	53	0.960	53	0.662
Baseline vs 3 years	50	0.561	50	0.113
Baseline vs 5 years	46	0.643	46	0.711

n[1] = matched pairs (Wilcoxon signed ranks). Each patient served as his or her own control. Missing data that reduced the number of paired observations (n) in each test are shown in the table.

Table 8 Pain pressure threshold (PPT) between groups

	Dercum Operated		Abdominoplasty Patients		Dercum Controls		Difference in Change Over Time*			
							Dercum Operated vs Abdominoplasty Patients		Dercum Operated vs Dercum Controls	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	Mean (95% CI)	*P* Value	Mean (95% CI)	*P* Value
Knee (mean)										
Baseline	29	11.9 (4.8)	41	38.8 (9.8)	58	14.9 (6.8)	Reference		Reference	
3 months	28	20.0 (8.9)	40	39.4 (9.7)	58	14.8 (7.8)	0.89 (–6.0 to 7.8)	0.80	7.9 (4.6 to 11.3)	<0.001
1 year	28	20.3 (9.1)	38	40.7 (9.9)	58	15.4 (8.3)	0.35 (–6.6 to 7.3)	0.92	7.6 (4.3 to 11.0)	<0.001
2 years	27	20.5 (8.5)	38	43.4 (13.0)	53	16.2 (10.9)	–1.5 (–8.5 to 5.4)	0.67	7.6 (4.2 to 11.0)	<0.001
3 years	28	21.8 (10.9)	37	42.9 (11.7)	50	17.0 (10.2)	0.036 (–6.9 to 7.0)	0.99	8.3 (4.9 to 11.6)	<0.001
5 years	28	20.3 (8.3)	35	41.8 (11.1)	46	16.6 (10.5)	–0.12 (–7.1 to 6.8)	0.97	7.0 (3.6 to 10.4)	<0.001
Abdomen (mean)										
Baseline	28	12.6 (4.1)	41	40.2 (9.8)	58	16.3 (7.9)	Reference		Reference	
3 months	27	23.1 (8.2)	40	39.4 (10.3)	58	16.3 (8.8)	10.0 (3.6 to 16.5)	0.003	9.7 (6.5 to 12.9)	<0.001
1 year	27	24.9 (8.9)	38	44.3 (11.8)	58	16.5 (8.8)	7.7 (1.2 to 14.2)	0.020	11.4 (8.1 to 14.6)	<0.001
2 years	26	24.9 (8.7)	38	48.5 (13.5)	53	17.5 (10.0)	3.6 (–2.8 to 10.1)	0.27	10.6 (7.3 to 13.8)	<0.001
3 years	27	24.5 (7.8)	37	48.2 (12.1)	50	19.1 (10.5)	3.6 (–2.9 to 10.1)	0.28	9.4 (6.1 to 12.6)	<0.001
5 years	27	23.4 (8.2)	36	49.3 (13.5)	46	17.7 (9.1)	1.9 (–4.7 to 8.4)	0.57	9.4 (6.1 to 12.7)	<0.001

* Mixed model analysis adjusting for age, BMI, and baseline PPT. Missing data that reduced the number of observations (n) in each test are shown in the table.
SD = standard deviation; CI = confidence interval; BMI = body mass index.

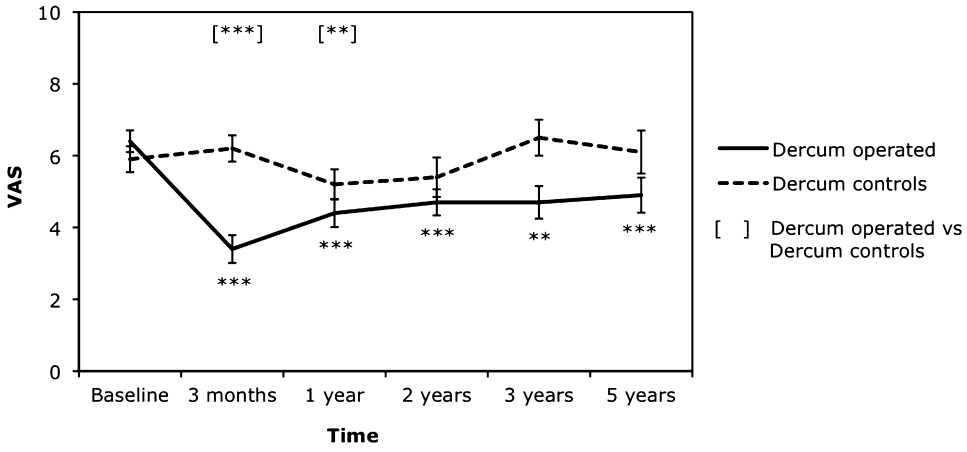

Figure 2 Pain intensity. The visual analog scale (VAS) values are given as mean ± SEM. Maximum VAS value is 10. Mean significances within the groups depict difference in change over time from baseline and are shown adjacent to respective error bars. Significances between the groups depict difference in change over time from baseline and are shown in the upper part of the figure. * $P = 0.05$, ** $P = 0.01$, *** $P = 0.001$. Only significant differences are shown.

has proposed that the sympathetic nervous system may cause the pain experienced in disorders of painful adipose tissue disease. The pain is thought to be generated by means of signals to the spinal cord from abnormal connections that have arisen between peripheral autonomic and sensory nerves [24]. Tentatively, liposuction avulses not only the sensory nerves but also these abnormal nerve connections. However, the fraction of nerves that is undamaged during liposuction reasonably also comprises a portion of the abnormal connections, and this might explain why the patients' pain is relieved but not completely eliminated after liposuction. Moreover, new abnormal connections might arise, which could explain why the patients in our study regain some of the pain a few years postoperatively. Furthermore, the mechanism could be supported by the fact that intravenous administration of lignocaine relieves the pain in patients with Dercum's disease temporarily [2,3,23,25,26], as inhibition of abnor-

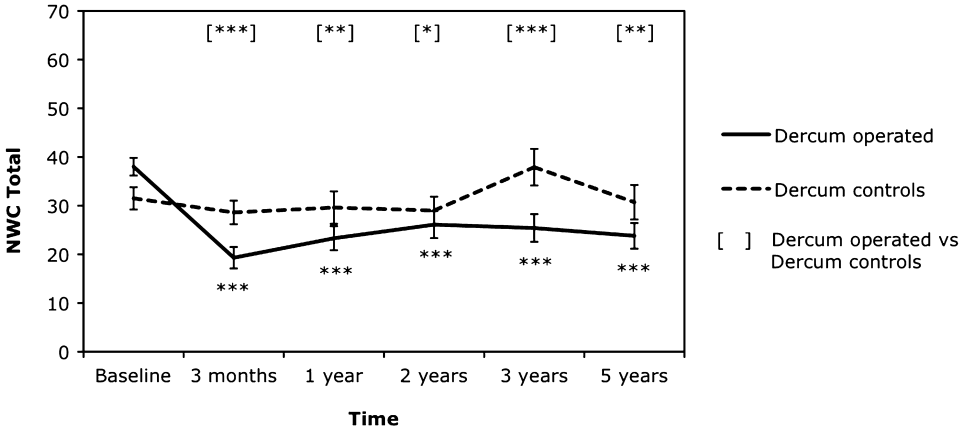

Figure 3 Number of words chosen (NWC). The NWC values are given as mean ± SEM. Mean significances within the groups depict difference in change over time from baseline and are shown adjacent to respective error bars. Significances between the groups depict difference in change over time from baseline and are shown in the upper part of the figure. * $P = 0.05$, ** $P = 0.01$, *** $P = 0.001$. Only significant differences are shown.

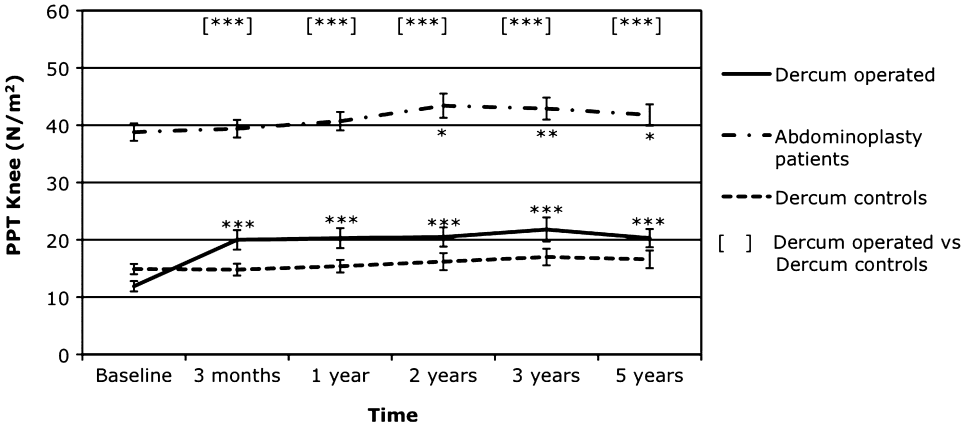

Figure 4 PPT for the knee. The PPTs are given as mean ± SEM. Significances within the groups depicts difference in change over time from baseline and are shown adjacent to respective error bars. Significances between the groups depict difference in change over time from baseline and are shown in the upper part of the figure. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Only significant differences are shown.

mal nervous impulse circuits previously has been put forward as a plausible explanation for the effect of lignocaine [23].

There is a considerable association between the effect of treatment and its outcome and patient expectations when chronic pain is treated [27,28]. Furthermore, it has been shown that surgery can evoke a placebo response, including both subjective change and objective effect [29]. However, the magnitude and the duration of the placebo effect have varied considerably between different studies [30]. A review on the placebo theory made by Koshi and Short [30] found one study demonstrating a duration of the placebo response up to 1 year [31] and another up to 5 years [32]. Several studies have demonstrated that the placebo analgesic effect across all individuals is of the magnitude 2 out of 10 on a VAS [30]. Furthermore, the diminishing number of the subjects that thought the operation had decreased their pain (Figure 6) can indicate that there could be a placebo response involved. Nonetheless, the marked effect of liposuction in our patients and the fact that the effect was stable over a long period could indicate that liposuction results in a true treatment effect. However, the mechanism by which liposuction diminishes the pain in Dercum's disease remains unclear.

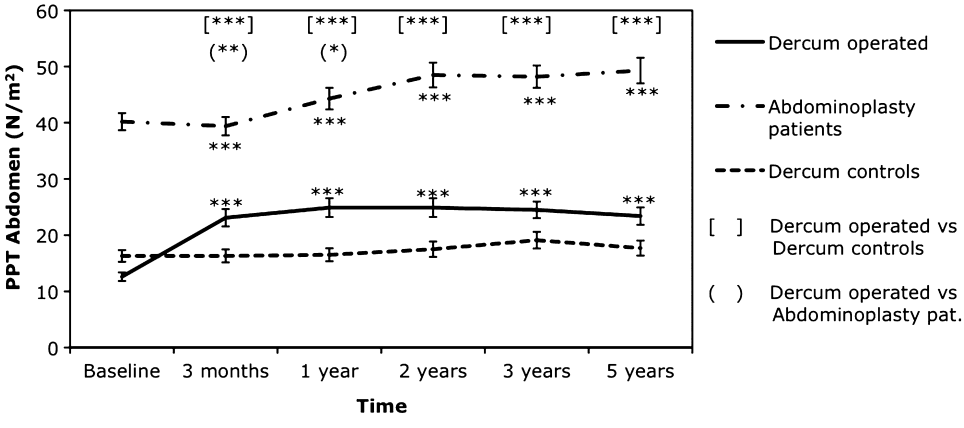

Figure 5 Pressure pain threshold (PPT) for the abdomen. The PPTs are given as mean ± SEM. Mean significances within the groups depict difference in change over time from baseline and are shown adjacent to respective error bars. Significances between the groups depict difference in change over time from baseline and are shown in the upper part of the figure. * $P = 0.05$, ** $P = 0.01$, *** $P = 0.001$. Only significant differences are shown.

Figure 6 The answer to the question "Did the operation decrease your pain?" is presented in percent.

It is thus difficult to determine whether the pain relief experienced is due to specific efficacy of the treatment. There are also other factors that have to be considered, such as the natural history of the disease and the phenomenon of regression to the mean [33]. In fact, there has been little research conducted on the natural history of Dercum's disease, but case reports have suggested that the pain might be aggravated over time [34]. However, this is not clearly supported by the measurements in our control group (Tables 4–9). Regression of the mean is a measurement error and can be described as the tendency to score closer to the mean the second time a measurement is performed [35].

Conclusion

In conclusion, our results suggest that liposuction might alleviate pain in patients with Dercum's disease for a period of at least 5 years. However, it is difficult to determine whether the effect is due to the actual surgery or to other factors. Furthermore, it is unclear how clinically significant the improvement is. Due to these unclearities and that not all patients experienced a clear pain relief after liposuction, future studies, including randomization and validated diagnostic criteria, are needed before liposuction can be considered the treatment of choice.

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References

1 Dercum FX. A subcutaneous connective tissue dystrophy of the arms and back, associated with symptoms resembling myxaedema. University Medical Magazine (Philadelphia) 1888;1:1–11.

2 Iwane T, Maruyama M, Matsuki M, Ito Y, Shimoji K. Management of intractable pain in adiposis dolorosa with intravenous administration of lidocaine. Anesth Analg 1976;55:257–9.

3 Atkinson RL. Intravenous lidocaine for the treatment of intractable pain of adiposis dolorosa. Int J Obes 1982;6:351–7.

4 Berenguer B, de la Cruz L, de la Plaza R. Liposuction in atypical cases. Aesthetic Plast Surg 2000;24:13–21.

5 De Silva M, Earley MJ. Liposuction in the treatment of juxta-articular adiposis dolorosa. Ann Rheum Dis 1990;49:403–4.

6 DeFranzo AJ, Hall JH, Jr, Herring SM. Adiposis dolorosa (Dercum's disease): Liposuction as an effective form of treatment. Plast Reconstr Surg 1990;85:289–92.

7 Scheinberg MA, Diniz R, Diamant J. Improvement of juxtaarticular adiposis dolorosa by fat suction. Arthritis Rheum 1987;30:1436–7.

8 Wollina U, Goldman A, Heinig B. Microcannular tumescent liposuction in advanced lipedema and Dercum's disease. G Ital Dermatol Venereol 2010; 145:151–9.

9 Kling D. Juxta-articular adiposis dolorosa, its significance and relation to Dercum's disease and osteoarthritis. Arch Surg 1937;34(4):599–630.

10 Fidanza F, Keys A, Anderson JT. Density of body fat in man and other mammals. J Appl Physiol 1953;6: 252–6.

11 Gaston-Johansson F. Measurement of pain: The psychometric properties of the Pain-O-Meter, a simple, inexpensive pain assessment tool that could change health care practices. J Pain Symptom Manage 1996;12:172–81.

12 Jensen M, Karoly P. Self-report scales and procedures for assessing pain in adults. In: Turk D, Melzak R, eds. Handbook of Pain Assessment. New York: The Guildford Press; 1992:19–44.

13 Melzack R. The McGill Pain Questionnaire: Major properties and scoring methods. Pain 1975;1:277–99.

14 Gaston-Johansson F, Hofgren C, Watson P, Herlitz J. Myocardial infarction pain: Systematic description and analysis. Intensive Care Nurs 1991;7:3–10.

15 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.

16 Bigatti SM, Cronan TA. A comparison of pain measures used with patients with fibromyalgia. J Nurs Meas 2002;10:5–14.

17 Bird SB, Dickson EW. Clinically significant changes in pain along the visual analog scale. Ann Emerg Med 2001;38:639–43.

18 Perry F, Heller PH, Levine JD. Differing correlations between pain measures in syndromes with or without explicable organic pathology. Pain 1988;34:185–9.

19 Nussbaum EL, Downes L. Reliability of clinical pressure-pain algometric measurements obtained on consecutive days. Phys Ther 1998;78:160–9.

20 Ohrbach R, Crow H, Kamer A. Examiner expectancy effects in the measurement of pressure pain thresholds. Pain 1998;74:163–70.

21 Takahashi K, Taguchi T, Itoh K, et al. Influence of surface anesthesia on the pressure pain threshold measured with different-sized probes. Somatosens Mot Res 2005;22:299–305.

22 Hansson E, Svensson H, Rosén I, Brorson H. Thermal and vibratory thresholds do not differ after liposuction in patients with Dercum's disease. J Plastic Surg Hand Surg 2010 (in press).

23 Petersen P, Kastrup J. Dercum's disease (adiposis dolorosa). Treatment of the severe pain with intravenous lidocaine. Pain 1987;28:77–80.

24 Dalziel K. The nervous system and adipose tissue. Clin Dermatol 1989;7:62–77.

25 Desai MJ, Siriki R, Wang D. Treatment of pain in Dercum's disease with lidoderm (lidocain 5% patch): A case report. Pain Med 2008;9:1224–6.

26 Juhlin L. Long-standing pain relief of adiposis dolorosa (Dercum's disease) after intravenous infusion of lidocaine. J Am Acad Dermatol 1986;15:383–5.

27 Linde K, Witt CM, Streng A, et al. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. Pain 2007;128:264–71.

28 Turner JA, Deyo RA, Loeser JD, Von Korff M, Fordyce WE. The importance of placebo effects in pain treatment and research. JAMA 1994;271:1609–14.

29 Beecher HK. Surgery as placebo. A quantitative study of bias. JAMA 1961;176:1102–7.

30 Koshi EB, Short CA. Placebo theory and its implications for research and clinical practice: A review of the recent literature. Pain Pract 2007;7:4–20.

31 McRae C, Cherin E, Yamazaki TG, et al. Effects of perceived treatment on quality of life and medical outcomes in a double-blind placebo surgery trial. Arch Gen Psychiatry 2004;61:412–20.

32 Marchand S, Kupers RC, Bushnell MC, Duncan GH. Analgesic and placebo effects of thalamic stimulation. Pain 2003;105:481–8.

33 Hoffman GA, Harrington A, Fields HL. Pain and the placebo: What we have learned. Perspect Biol Med 2005;48:248–65.

34 Moi L, Canu C, Pirari P, et al. [Dercum's disease: A case report]. Ann Ital Med Int 2005;20:187–91.

35 Kelley JM, Boulos PR, Rubin PA, Kaptchuk TJ. Mirror, mirror on the wall: Placebo effects that exist only in the eye of the beholder. J Eval Clin Pract 2009;15:292–8.