

Risk factors and complications after body-contouring surgery and the amount of stromal vascular fraction cells found in subcutaneous tissue

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Abstract

Body contouring surgery following massive weight loss is often prone to complications. Subcutaneous adipose tissue is a rich source of stromal vascular fraction (SVF) cells, and moreover it plays an important role in the pathophysiology of obesity, metabolic syndrome, and wound healing. In this retrospective, single-centred appraisal, complications are examined and correlated with individual SVF numbers in abdominal subcutaneous fat tissue. We analysed whether the weight loss method affected complications. Eighty seven massive weight loss patients undergoing body contouring surgery between 2010 and 2017 were included in the study. In total, 57 cases with at least one complication were recorded (65.5%). Maximum lifetime weight was 109.6 kg (range 48–184 kg). Half of the complications (50.8%) were minor complications without the need for surgical revision. The mean number of SVF found in the resected tissue was 714 997.63 cells/g fat tissue. We found no statistical difference in complication rates dependent on cell numbers. Smoking ($P = .049$) and a high BMI at the time point of surgery ($P = .031$) led to significantly more complications. Also, a high resection weight ($P = .057$) showed a tendency for impaired wound healing. However, there was no difference in complication rates following body contouring procedures attributable to the method of weight loss in this study.

KEY WORDS

ASC, body contouring, Clavien-Dindo, postbariatric, SVF

1 | INTRODUCTION

Knowledge about the stromal vascular fraction (SVF) and thus, adipose-derived stem cell (ASC) physiology is of paramount interest in regenerative medicine and plastic surgery since many potential uses for clinical application have been described. Mostly, translational research puts its focus and efforts on applications of multipotent ASCs that are widely known to be important in wound healing.^{1,2} These cells make up for about two-thirds of the CD45-negative cells within the

SVF, which is thus representative for the amount of ASCs in the tissue, and there is no difference in cell yield between superficial and deep subcutaneous fat layers.³ Recent literature suggests that the therapeutic effect of ASCs is partially mediated by the secretion of cytokines, and thus they are able to stimulate local fibroblasts of the wound bed^{4,5} to promote wound healing and angiogenesis.⁶ Also, in problematic diabetic wounds, ASCs have been shown to accelerate wound healing in animal models⁷ via enhanced angiogenesis and immunomodulation.⁸ Most authors therefore promote the

local application of ASC to exert positive influence on wound healing physiology.⁹ However, the knowledge about therapeutic application of the SVF and ASC in humans is still limited, and the use of ASC-enriched autologous fat grafts¹⁰ is not routine until today.¹¹

Massive weight loss patients suffer from skin excess, which leads to mechanic irritation, intertrigo, or ulceration, and can be prone to infection.¹² Patients are affected in daily life and social interactions and may suffer from psychological impairment.¹³ Redundant skin and soft tissues are corrected employing body-contouring surgery. Although most patients require the correction of skin excess of the trunk, extremities might be affected as well.¹⁴ However, body-contouring procedures have been shown to be prone to complications, and complication rates are reported to be up to 80% throughout the literature.¹⁵ Common complications are delayed wound healing, secondary wound dehiscence, postoperative haematoma, or seroma.¹⁶ Bariatric surgery leads to nutritional deficiencies that result from anatomical changes in the gastrointestinal system. Herein, protein deficiencies can slow down cell proliferation as well as extracellular matrix protein production, and thus wound healing and angiogenesis.¹⁷ Up to 35% of bariatric patients suffer of folate and vitamin B12 deficiency, while especially gastric bypass patients suffer from iron deficiency.^{18,19} Despite malnutrition in postbariatric patients,^{20,21} it could be shown that complication rates of body-contouring surgery do not vary depending on the weight loss method.^{22,23} Finally, it has been shown that SVF content and ASC behaviour are altered in the subcutaneous tissue of morbid obese patients,²⁴ and these changes are not completely restored after bariatric surgery-induced weight loss. Thus, we hypothesised that altered SVF content in the subcutaneous tissue of postbariatric patients is affecting the regenerative effects of wound healing and is therefore linked to an increased complication rate in postbariatric body-contouring procedures compared with patients that lose weight by means of lifestyle change.

In this single-centred appraisal, we aimed to analyse complications of body-contouring procedures depending on the weight loss method. Moreover, we isolated the SVF from the resected subcutaneous tissue of all patients. We studied whether the method of weight loss affects the amount of SVF cells found in the tissue and whether a decreased SVF cell number is connected to a higher complication rate.

2 | MATERIAL AND METHODS

Data from patients scheduled for elective body-contouring surgery in our department during the period from June 2010 to October 2017 were retrospectively reviewed in our electronic medical record database. Patients who underwent abdominoplasty or lower body lift after either weight loss by

Key Messages

- body contouring surgery following massive weight loss is often prone to high complication rates
- the purpose of the study was to analyse the complication rates after body contouring in postbariatric patients, individual patients risk factors, and stromal vascular fraction (SVF), and thus adipose-derived stem cells in the resected tissue
- smoking, a high BMI at the time point of operation, and a high resection weight lead to significantly more complications after body contouring surgery
- the method of weight loss does not affect overall complication and wound healing complication rates independent of whether patients had postbariatric surgery or lost weight by lifestyle change only
- the amount of SVF in the subcutaneous tissue is not altered by weight loss that is achieved by bariatric surgery even though it was shown in the literature that cells have an altered secretome and differentiation potential in postbariatric patients

lifestyle change or by bariatric surgery were eligible for the study. All patients were asked to provide their written informed consent for isolation of the SVF/ASC cell population in our laboratory, which was approved by the Ethics Committee of the Medical University of Innsbruck (UN4368, EK 301/4.5; AN2014-0244, EK 341/4.9, EK 388/5.5; AN4368-30145, EK 301/4.5, and EK 397/5.8). We grouped the patients according to the weight loss method into the group of postbariatric patients or the group of lifestyle-change patients. The reviewed data included age, BMI, maximum lifetime weight, amount of weight loss, smoking, comorbidities, and former abdominal surgery. Moreover, duration of hospital stay, complications, and follow up were recorded. Complications were rated according to the widely used Clavien-Dindo classification,^{25,26} which has been validated for bariatric patients²⁷ before. Postbariatric patients were subjected to subgroup analysis dividing the group into gastric band patients and gastric bypass patients. Only one patient had received a gastric sleeve resection and was excluded from further analyses.

2.1 | Isolation and cell counting of human ASCs

ASCs were isolated from subcutaneous abdominal fat tissue obtained from patients (n = 87; 87% female, 13% male)

undergoing elective body-contouring surgery in our department. For ASC isolation, adipose tissue was washed with phosphate-buffered saline (PBS), minced into pieces, and incubated with collagenase type I (0.15% in PBS, Roche, Germany) for 1 hour at 37°C. After collagenase digestion, samples were centrifuged at 500g for 10 minutes. Pelleted SVF was treated with erythrocyte lysis buffer (0.5 M NH₄Cl, 0.5 M KH₂PO₄, and 100 mM EDTA, Roth, Germany) for 10 minutes and spun at 500g for 10 minutes. The SVF pellet was resuspended in DMEM/F12 medium (Lonza, Austria), filtered through a 100 and 40 µm nylon mesh cell strainer (VWR, Austria), and counted with a CASYTM cell counter (Schärfe System, Germany).

2.2 | Statistics

To assess the quality of data, descriptive statistics were performed. Data are presented as mean ± SD if not indicated differently. Normally distributed data were analysed by unpaired student's *t* test while the Mann-Whitney *U* test was applied for non-parametric data. *P* values of <.05 were considered statistically significant. In order to facilitate analysis, SVF cell number data were log transformed. Pearson's chi-square test was used to compare the categorised data of independent subgroups, otherwise the Fisher's exact test was employed. One-way ANOVA was applied to correlate SVF cell number data with clinical data. All statistical analyses were carried out using the SPSS (IBM Statistics, V.21, Armonk) Statview statistics software (SAS Institute Inc, version 5.0.1) and Prism 5 (GraphPad software Inc, version 5.0).

3 | RESULTS

3.1 | Descriptive statistics

The study included 11 male (12.6%) and 76 female (87.4%) patients (total *n* = 87 patients), and mean patients' age was 39.5 years (range 21.8-71). The mean maximum weight before weight loss was 109.5 kg, and the mean maximum BMI before weight loss was 39.47 kg/m² (range 18.82-72.78 kg/m²). The mean recorded weight loss was 39.3 kg (range 0-112 kg) while mean resection weight was 1447 g (range 145-5200 g). Nine patients (10.3%) underwent lower body lift including belt lipectomy and medial thigh lift, while 78 (89.7%) patients had abdominoplasty. In total, 26 patients (29.9%) were active smokers at the time point of the operation, 6 (6.9%) patients were former smokers that reported to have quit smoking with a mean of 6 months before operation (range 13-0.3 months). All other patients reported to be non-smokers. With regard to other risk factors, 6 patients (6.9%) had diabetes type 2 while 45 (51.7%) patients had other metabolic diseases such as hypercholesterolemia or thyroid insufficiency. Six (6.9%)

patients suffered from arterial hypertension, and 51 (58.6%) patients had former abdominal surgery.

3.2 | Method of weight loss

Thirty-nine (44.8%) patients lost weight by lifestyle changes only while 48 (55.2%) patients underwent bariatric surgery. Of these, 14 patients had gastric banding, and only one patient was operated employing gastric sleeve resection and 33 patients had a gastric Roux-en-Y bypass. The single patient with gastric sleeve resection was excluded from the study.

3.3 | Complications and weight loss method

Almost half of the patients underwent bariatric surgery (55.2%) while the other group (44.8%) lost weight by lifestyle changes such as a healthy diet and sports. Overall, post-bariatric patients did not suffer from significantly more complications (*P* = .469), as depicted in Table 1. We could not identify a significant difference for postoperative haematoma (*P* = .125) postoperative lymph oedema of the region (*P* = .513), wound infection (*P* = .683), or minor wound-healing problems (*P* = .102) between the two groups. There was a positive tendency in postbariatric patients to show more seroma postoperatively, but no statistical significance could be revealed (*P* = .056).

3.4 | Complications according to Clavien-Dindo

In total, in 57 cases, at least one complication according to the Clavien-Dindo classification^{25,26} (excluding class 1 complications as follows) was recorded (65.5%) while 30 (34.5%) patients had a complication-free postoperative course and healing. These 30 patients were classified according to Clavien-Dindo class 1 during data analysis, which includes every deviation from the standard postoperative course such as the administration of antiemetics, analgetics, or physiotherapy. However, in patients after body-contouring surgery, such minimal interventions do not necessarily indicate a complication but are mandatory in standard postoperative care. Therefore, we consider these patients as complication free (*n* = 30, 34.5%). Clavien-Dindo class 2 was assigned to 29 patients (33.3%) including postoperative blood transfusion and antibiotics other than the standard single shot that is administered at the start of surgery. Fifteen patients (17.24%) were classified Clavien-Dindo 3a due to wound healing problems such as minor necrosis of wound margins, which were treated by reoperation in local anaesthesia. This includes the aspiration of seroma by puncture. A total of 13 patients (14.94%) had to be reoperated in general anaesthesia, mostly due to postoperative hematoma, massive wound dehiscence, or major wound

TABLE 1 Comparison of patients with or without complications with regards to age, gender, risk factors, and cell counts

	Complications	No complications	<i>P</i> value
Age	38.8 ± 11.8	39.6 ± 10.4	
Gender			.067
Male	8	3	
Female	49	27	
Smoking			.049*
Active smoker	19	6	
Quit before surgery	7	0	
Non-smoker	5	50	
Arterial hypertension	2	4	.951
Diabetes mellitus	0	6	.66
Metabolic disorder	28	17	.503
Former abdominal surgery	17	34	.927
BMI at surgery (kg/m ²)	25.78 ± 3	24.07 ± 2.5	
BMI > 25 at surgery (kg/m ²)	57	30	.031*
Body weight at surgery	71.8 ± 12.6	67.8 ± 9.4	.124
Resection weight (g)	1602.05 ± 1165.192	1135.5 ± 742.7	.057
SVF (cells/g tissue)	619 505.1 ± 8952	896 430.54 ± 9813	.137

Abbreviations: BMI, body mass index; SVF, stromal vascular fraction. **P* < .05.

healing problems (Clavien-Dindo class 3b). There were no life-threatening or deadly complications (Clavien-Dindo class 4 or 5). Postbariatric patients did not suffer from significantly more complications (*P* = .469). With regard to the weight loss method, more complications were recorded in the postbariatric group when excluding Clavien-Dindo class 1, but there was no significant difference to the lifestyle-change group (*P* = .102).

3.5 | Impact of individual patient-risk factors

In this clinical study, we aimed to identify risk factors for postoperative wound healing complications depending on individual risk factors and the weight loss method. In total, 57 (65.5%) patients with complications were documented as listed in Table 2. Of those, 36.5% had more than one complication. Overall, minor wound healing problems were the most common complication. Patients' medical records were assessed for individual risk factors. The maximum lifetime weight was mean 109.6 kg (range 48-184 kg). As expected, patients in the postbariatric group had a significantly higher maximum lifetime weight than in the lifestyle group (*P* = .021). A high absolute body weight at the time point of body-contouring surgery did not significantly increase the risk of postoperative complications (*P* = .124). In contrast, patients with a higher BMI at the time point of operation sustained significantly more wound healing complications than those with a normal BMI (*P* = .031), and among these,

TABLE 2 Comparison of patient groups regarding weight loss method, type of complication, and Clavien-Dindo classification

	Postbariatric group	Lifestyle group	<i>P</i> value
Complications (including °1)	67.40%	64.30%	.469
Clavien-Dindo °1	16	14	
Clavien-Dindo °2	18	11	
Clavien-Dindo °3a	9	6	
Clavien-Dindo °3b	8	5	
Clavien-Dindo °4	0	0	
Postoperative haematoma	6	2	.125
Surgical site infection	2	2	.683
Seroma	19	12	.056
Wound healing problem	34	22	.102
Lymphedema	3	4	.513

especially more seroma formation (*P* = .037) was seen. Body mass index at the time point of operation was the mean of 25.3 kg/m² (range 18.82-36.42). The total amount of weight loss was mean 39 kg (range 0-112 kg). In total, 25 patients (28.7%) were active smokers at the time point of the operation, 7 patients (8.05%) were former smokers that reported to have quit smoking with a mean of 6 months before operation (range 13-0.3 months). Patients who were active smokers or had quit smoking shortly before surgery

showed significantly more overall complications ($P = .049$) and wound healing problems ($P < .0001$) compared with non-smokers. Former abdominal surgery was not related to wound healing problems ($P = .891$). Patients with diabetes mellitus or arterial hypertension as well as other metabolic disorders such as hypercholesterolemia and thyroid insufficiency were not prone to more complications in this clinical study.

3.6 | SVF cell numbers in subcutaneous fat tissue after massive weight loss

We isolated the SVF containing the ASCs from the resected fat tissue of all patients and analysed SVF cell numbers comparing the total cell numbers per gram fat between patient groups. The mean SVF cell number was 714 997.63/g fat tissue in all patients. The patients in the complication group had a mean cell number of $619\,505.1 \pm 8952$ /g subcutaneous fat tissue while patients with a complication-free postoperative course showed mean SVF cell numbers of $896\,430.54 \pm 9813$ /g fat tissue. However, this difference was not tested to be significant ($P = .137$), thus analysing the log-transformed data in one-way ANOVA tables but with moderate interaction significance employing eta-square ($ES = 0.26$). When analysing SVF cell numbers of the post-bariatric patients (SVF cell number $\log^{10} = 5.45$) and the lifestyle patient group (SVF cell number $\log^{10} = 5.63$), no significant difference could be found ($P = .171$), suggesting only minor changes in this specific cell population in both bariatric and lifestyle change massive weight loss. Smoking did not have a significant effect on SVF cell numbers in subcutaneous tissue ($P = .150$); however, smokers were prone to more wound healing problems as described above.

4 | DISCUSSION

Body-contouring surgery has been shown to be prone to more complications than other aesthetic procedures and herein, complication rates up to 80% are reported in the literature.¹⁵ The usual complications include delayed wound healing, wound dehiscence, postoperative haematoma, and seroma.¹⁶ As it is well known that bariatric surgery leads to nutritional deficiencies resulting from anatomical changes in the gastrointestinal system, one is easily tempted to hypothesise that this might be the cause for the high complication rate. Employing this hypothesis, there were three major scopes of this study. First, we aimed to evaluate whether the method of weight loss does exert any influence on patient's outcome and complication rates. The second aim was to define the risk factors for complications after body-contouring surgery following massive weight loss. Finally,

we hypothesised that patients with low SVF numbers in subcutaneous fat tissue suffer more complications than others.

With regard to the method of weight loss (life style vs bariatric surgery), the data of our patient cohort showed no significant difference in overall complication rate ($P = .469$). Minor Clavien-Dindo class 1 events were not considered as complications because interventions such as antiemetics and physiotherapy are included in the clinics' standard postoperative care in body-contouring patients. This may be practiced differently in other countries where such a surgery is often done in an outpatient setting.^{28,29} Even after excluding Clavien-Dindo type 1 classified complications, no significant difference in the overall complication rate between the two groups was observed ($P = .102$). In total, 33% of all patients were assigned Clavien-Dindo class 2, which refers to a prolonged administration of antibiotics beyond single shot or the need for blood transfusion. However, only four patients suffered from surgical site infection leading to reoperation. It has been shown that surgical site infection is of higher incidence during the summer months,³⁰ and indeed, none of the patients in this cohort with evident surgical site infection has been operated during the cold months of the year from September to May. Also a high maximum lifetime weight, a high amount of weight loss prior to surgery, and high blood loss during surgery³¹ increase the risk for surgical site infections, all factors that typically apply for massive weight loss patients. Of all patients, 17.24% had to be reoperated using local anaesthetics because of minor wound healing problems or had to undergo seroma puncture (Clavien-Dindo class 3a). A comparable amount of patients (14.94%) underwent revision surgery in general anaesthesia (Clavien-Dindo class 3b). No life threatening complications were observed. In summary, bariatric patients did not suffer more complications than the patients from the lifestyle group, especially not more severe complications Clavien-Dindo °3 requiring surgical intervention. This reflects the results from other groups^{23,32} found in the literature. Surprisingly, our data do not support the hypothesis that patients do suffer more complications after undergoing bariatric surgery. In fact, outpatient check-ups of postbariatric patients are performed at close intervals in our clinic, and therefore, nutritional deficits can be easily detected and corrected in most cases. Hence, a history of bariatric surgery should not be considered a risk factor per se as demonstrated in this patient collective. However, a good compliance of the patient seems an absolute necessary feature.

In postbariatric patients, the mean resection weight was higher than in the lifestyle group without statistical significance ($P = .057$). However, a significant correlation was found between preoperative BMI and weight of resected tissue ($P = .031$) in concord with the results of other groups.^{23,32} Patients presented with a mean BMI of 25.3 kg/m² at the time point of surgery (range 36.42-18.82). Patients that had a

normal BMI ranging between 20 and 25 at this time point sustained significantly less wound healing complications than those with a higher BMI ($P = .031$). However, body contouring remains a valuable tool to improve life quality and to help restore a normal life style³³ that profits from a broad acceptance of the increased perioperative risk of complications among bariatric patients. From our data, it is not possible to draw a conclusion for body-contouring patients with an underweight BMI (<20) at the time point of operation because only three patients out of the whole study met this criterium; also we did not find any literature about this specific patient group, suggesting a need for research on this topic. Absolute body weight at the time point of operation did not affect complication rate negatively ($P = .124$), emphasising the usefulness of the body mass index formula compared with simple weight monitoring. Weight loss took a mean 34 months (range 0-129 months) of time. Patients who needed longer to lose weight had significantly less complications ($P = .042$), indicating a more enduring effect, an overall healthier lifestyle, and hence, the importance of behavioural factors.³⁴

With regard to lifestyle, patients who were active smokers or quit smoking within few months before the operation suffered significantly more wound healing complications ($P = .049$) than non-smokers. To further reduce this risk, smoking status of patients could be controlled using cotinine serum levels,³⁵ which has also been suggested in free flap surgery.³⁶ However, the cotinine test provides quantitative information about smoking up to 4 days before testing and thus would have to be done repeatedly because our data suggest that smoking cessation at least 6 months before surgery is mandatory to reduce the risk of complications. Among the widely known negative effects of cigarette smoke on wound healing,³⁷ it has been shown in vitro that cigarette smoke impairs ASC vasculogenic activity in fat tissue that might contribute to this effect.

Although most authors promote the local application of ASC to exert positive influence on wound healing physiology,⁹ it has been shown that the cells of morbid obese patients show an altered secretome during induced differentiation in vitro compared with cells from healthy individuals. Even more interestingly, these changes are not restored after bariatric surgery,²⁴ implicating a life-long impairment of regenerative effects of ASC in these patients. In our work, we studied whether overall cell number of the SVF is altered in postbariatric patients. After the cell isolation procedure was carried out, we calculated the number of cells per gram fat tissue hypothesising that massive weight loss changes cellularity of the SVF. It has been shown before that other disorders of the fat tissue like lipedema do significantly change the yield of cells in SVF isolation compared with healthy individuals.³⁸ Also, we were able to show different cell yields in a representative sample of the patients in

this study when processing superficial abdominal subcutaneous adipose tissue separately from the adipose tissue found deep to Scarpa's fascia as published elsewhere,³ which proves the versatility of subcutaneous tissue and its compartments on an intraindividual basis. Herein, other authors showed that weight loss is taking place to a different extent in the superficial and deep layers of abdominal subcutaneous fat tissue in bariatric versus lifestyle weight loss.³⁹ However, despite a slightly decreased total SVF cell number per gram fat tissue, we could not find a significantly altered cell yield in postbariatric patients compared with the lifestyle group ($P = .137$). This implicated that the total SVF cell numbers are not altered, notwithstanding the changes in subfractions that have been shown by other authors.²⁴ It should be noted that despite being of routine use, the SVF isolation method⁴⁰ has some limitations that could influence the cell yield such as the procedure being carried out by different members of staff in the laboratory, with the use of different charges of collagenase solution over the years. Cell yield is also sensitive to small changes such as temperature variations or mechanic handling,⁴¹ which might be uncontrollable and even unnoted under certain circumstances.

Considering the postoperative complication rate, patients with lower cell numbers did suffer from complications more frequently but this trend was not tested significant either ($P = .123$) relativising the role of locally available ASC in wound healing. Also, this might suggest a different secretory behaviour of ASCs in their locoregional niche compared with the wound healing enhancement that is experienced in the different applications of free autologous lipofilling,¹⁰ where cells are transferred to a different wound bed or tissue. However, further research in this specific field is needed.

5 | CONCLUSION

In summary, we could not detect a higher rate of overall complications in postbariatric patients compared with patients who lost weight by life style change only, which is in concord with the results published recently by two other groups.^{23,32} Looking at the type of bariatric surgery, there was no subgroup of patients that seems especially prone to complications (both minor and major), suggesting that the individual risk of body-contouring surgery after massive weight loss should be evaluated carefully in each case. The amount of SVF cells, and thus ASCs, in the subcutaneous tissue of the abdomen is not significantly altered in postbariatric patients compared with patients that lost weight by lifestyle changes. Smoking or former smoking until shortly before operation is independent individual risk factor that leads to an increased complication rate, and thus repeated testing for cotinine could be useful in monitoring patients' smoking status. Moreover, a high BMI at the time point of operation and a high

resection weight are associated with increased wound healing problems. Irrespective of age, maximum lifetime body weight or former abdominal surgery, both weight loss groups had equal complication rates of postbariatric body-contouring surgery, suggesting that nutritional deficiencies in malabsorption after bariatric surgery do not significantly affect the outcome of body contouring as long as they are properly substituted. Therefore, careful monitoring and adequate medication are of paramount interest for the preparation and follow-up for body-contouring surgery in this type of patients.

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