

Improving Abdominal Plastic Scars with a Dietary Supplement—A Comparative Study

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Introduction: Massive weight loss following bariatric surgery has a major functional and aesthetic impact on patients. Many patients are nonetheless reluctant to undergo plastic surgery in connection with their former obesity because they fear potentially large scars, even though such scars are not visible (ie, they are covered by undergarments).

Purpose: The aim of this study was to evaluate the quality of wound healing in patients receiving Celergen supplementation following abdominoplasty, compared with a control group. The hypothesis was that supplementation would speed up wound healing and improve scar quality.

Materials and Methods: We conducted a prospective, monocentric, controlled study of patients undergoing abdominoplasty. A group of patients received Celergen, a food supplement, for 3 months and were monitored for 1 year after their surgery.

Results: Of 33 patients who underwent abdominoplasty, 25 received Celergen supplements. There was no significant difference between the 2 groups. The mean time to wound healing was significantly better in the group receiving supplementation compared with the control group [respectively, 24.6 ± 9.31 days and 34 ± 13.48 days (P = 0.03)]. The Patient and Observer Scar Assessment Scale (POSAS) observer score was significantly better at 1 year in the group receiving supplementation compared with the control group [12.68 \pm 6.6 and 17.38 \pm 5.24 (P = 0.01), respectively]. There was no significant difference in the total POSAS score at 1 year (P = 0.166).

Conclusion: Celergen supplementation significantly improved the time to healing and the POSAS observer score at 1 year for patients undergoing abdominoplasty. (*Plast Reconstr Surg Glob Open 2018;6:e1907; doi: 10.1097/GOX.000000000001907; Published online 4 October 2018.*)

INTRODUCTION

Obesity is defined as abnormal or excessive fat accumulation with significant physical and psychological impacts. Overweight among adults refers to a body mass index (BMI) of between 25 and 29 kg/m^2 while obesity refers to a BMI greater than or equal to $30 \text{ kg/m}^{2.1}$

In terms of prevalence, in 2015 obesity in France was estimated to affect 17% of the population aged 18-74 years.² Between 1975 and 2016, the worldwide prevalence

From the Service of Plastic, Reconstructive and Aesthetic Surgery, and Maxillo-facial Surgery, Henri Mondor's Hospital, Créteil Cedex. Received for publication June 13, 2018; accepted June 27, 2018. Boxes of Celergen were provided for use during this study.

Copyright © 2018 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal. DOI: 10.1097/GOX.00000000001907 of obesity tripled, with 39% of the global population aged 18 years and over being overweight in 2016.¹

Due to the relative difficulty of successfully losing weight through diet and physical activity alone and in light of the improvements made to bariatric surgery techniques, there has been a rise in surgical procedures.^{3,4} The various restrictive surgical techniques for sleeve gastrectomy, and malabsorptive diversion techniques such as gastric bypass, frequently result in inadequate nutrition and nutritional deficiency that may lead to complications such as anemia and osteoporosis.^{3,5}

Following obesity surgical procedures, massive weight loss leads to excess loose skin that causes considerable functional and aesthetic discomfort and may lead to conditions such as mycoses, macerated skin, and itching. These factors prompt many patients to seek postbariatric surgery.

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Despite the fact that abdominoplasty incisions are not visible because they are hidden by undergarments, many patients are reluctant to undertake such surgery out of fear of potential scarring. Moreover, these patients present a higher risk of complications than other patient populations.⁷⁻⁹

Wound healing is not as good among these patients, who often have poor nutrition.¹⁰ The findings of a study involving 100 patients showed that 13.8% of them had hypoalbuminemia, whereas 40% showed evidence of iron deficiency and 14.5% had vitamin B12 deficiency. Impaired fasting glucose was observed in 6.2% of the patients.¹¹ Yet good nutritional status is essential for effective wound healing to take place. Glucose provides the body with an energy source for angiogenesis, fatty acids are essential for healthy cell structure and for the inflammatory process to take place, and finally proteins are necessary for collagen synthesis and formation.¹² Protein supplementation may therefore improve the aesthetics of wound healing.

The efficacy of a number of nutritional supplementations has already been demonstrated in the healing of various types of wounds. Some wounds such as eschars, acute and chronic diabetic ulcers, and venous ulcers may show significant improvement with supplementation of nutrients such as arginine, vitamin C, zinc, and camel milk proteins.^{13–18}

It is therefore necessary during surgical procedures such as abdominoplasty, which causes long scars, to ensure that patients receive holistic care that includes, if necessary, food supplementation in addition to surgery.

A study based on a wound healing in vitro model has shown that Celergen, a marine-derived food supplement, led to increased fibroblast growth and collagen secretion in the tissues receiving supplementation, and increased migration to injured tissue.¹⁹ Collagen provides the matrix for tissue regeneration and wound healing, and the migration of fibroblasts into the collagen triggers the induction of angiogenesis. In addition, fibroblasts preserve the structure of connective tissue.^{20,21} It was also shown that Celergen had an antioxidant protecting effect on skin fibroblasts.²²

The aim of this prospective study was to evaluate the duration and the quality of wound healing in patients receiving Celergen supplementation following abdominoplasty, compared with a control group. The hypothesis was that supplementation would speed up wound healing and improve scar quality.

MATERIALS AND METHODS

Study Design

A prospective, monocentric, controlled, randomized study was conducted between May 2016 and December 2016 at the Department of Plastic, Reconstructive, Aesthetic and Maxillofacial Surgery of the Henri Mondor Hospital in Créteil, France.

Patients

After signing an informed consent form, patients of both sexes, aged 18 and over, who were to undergo abdominoplasty following weight loss were included in the study. The conditions of supplementation, doses, treatment contraindications (fish allergies) and the aim of the study were presented and explained to patients.

Food Supplementation with Celergen

Patients in the experimental group received supplementation with Celergen, a food supplement manufactured by Swiss Caps (composition per capsule: marine protein 300 mg, peptide E collagen 230 mg, hydro MN peptide 40 mg, lutein 10 mg, grape skin extract 10 mg, coenzyme Q_{10} 10 mg, selenium 50 µg). All patients started supplementation the day before surgery, taking 1 capsule in the evening on an empty stomach. They continued taking 1 capsule daily in the morning before breakfast for 3 months after surgery.

During follow-up consultations, patients were asked to confirm that they had taken the food supplement each day. Capsules were packaged in single-dose units, and supplements were distributed to patients in 3 boxes containing 30 capsules each. Upon enrollment in the study, patients were informed that if they forgot a capsule, it could be taken later during the same day (on an empty stomach) or the next morning, together with that day's dose.

All patients (100%) stated that they had taken all the supplements in compliance with our study protocol. However, we have no objective evidence of treatment adherence.

Patient Management

All patients undergoing an abdominoplasty procedure performed by the same surgeon between May 2016 and December 2016 were included in the study. The sealed envelope system of randomization was used to allocate patients into 2 groups: with and without food supplementation. The surgical procedure was then performed. Deep quilting sutures were made to relieve tension on the skin suture and to reduce the risk of seroma. Each patient received the same type of stitches. A dermo-hypodermic overlock stitch was made using resorbable braided 3/0 thread, followed by an intradermal overlock stitch of resorbable 3/0 polysaccharide thread. Compressive dressing was applied immediately after surgery and removed the next day. An abdominal support belt had to be worn day and night for 6 weeks.

Inclusion criteria were undergoing abdominoplasty performed by the head of the study between May and December 2016, being at least 18 years old.

Exclusion criteria were being under age 18, having fish allergies, being operated on by a surgeon other than the head of the study, and not complying with the food supplement regimen.

Clinical Evaluation and Patient Follow-up

Patients were monitored on a weekly basis during follow-up consultations until complete healing of the surgical wound, that is, until full epidermization and the total disappearance of scabs, so that wound dressing was no longer necessary. After that, follow-up consultations were scheduled at 1 month, 3 months, and 6 months. The primary endpoint was time to complete wound healing.

Secondary endpoints were scar quality at 1 year, assessed using a validated scale, the Patient and Observer Scar Assessment Scale (POSAS)^{23,24} and complications (hematoma, infection, seroma, wound dehiscence).

The demographical data collected included age, sex, BMI, smoking status, and complementary procedures performed during the surgery.

This study was conducted in compliance with the Declaration of Helsinki of October 2013 concerning biomedical research. It was approved by a local institutional review board.

Statistical Analysis

A descriptive analysis was used for demographical data. Variables were represented as mean \pm SD. Means were compared using the Student's *t* test. The Shapiro Wilk test was used to assess normality of the distribution of the variables. All *P* < 0.05 values were considered to be statistically significant. GraphPad Version 6 software was used for graphics and statistical analyses.

RESULTS

Patients

Following massive weight loss, 33 patients underwent abdominoplasty. Among this group, 25 patients received supplementation with Celergen (24 women and 1 man; mean age, 44.45 ± 10.5 years). Five women were prematurely excluded from the study due to noncompliance with the supplementation regimen. Eight patients made up the control group. They were not asked to follow a specific diet (7 women and 1 man; mean age, 40.7 ± 7.85 years). Patient characteristics appear in Table 1.

There was no significant difference between the 2 groups in terms of age, sex, BMI, smoking status, and medical history (Table 1).

The mean time to wound healing corresponding to full epidermization and discontinuation of wound dressing was significantly reduced in the study group compared with the control group (24.6 ± 9.31 days for the group receiving supplementation and 34 ± 13.48 days for the control group P < 0.03; Fig. 1).

Table 1. Demographic Characteristics of the 2 Groups

	Control Group	Group Receiving Celergen	Р
Age	40.7 ± 7.85	44.45 ± 10.5	0.215 (NS)
BMI	26.2 ± 4.87	25.53 ± 3.04	0.672 (NS)
Sex (W/M)	7/1	19/1	0.50 (NS)
Smoking status (S+/S-)	2/6	2/18	0.55 (NS)
History			
Diabetes	1	1	0.50 (NS)
HTN	1	4	0.99 (NS)
Method to lose weight			1 (NS)
Sleeve gastrectomy	6	15	1 (NS)
By-pass	2	4	1 (NS)
Gastric band	0	1	1 (NS)

Results: Mean \pm SD. P: Student's *t* test.

HTN, hypertension; NS, not significant.



Fig. 1. Time to wound healing.

The POSAS observer score at 1 year was significantly better in the group receiving supplements (POSAS observer score = 12.68 ± 6.6) compared with the control group (PO-SAS observer score = 17.38 ± 5.24 ; P = 0.01). However, there was no significant difference between the 2 groups for the POSAS patient score (20.69 ± 9.24 and 22.25 ± 7.82 , respectively, for the experimental and the control groups; Fig. 2).

Our findings showed no significant difference for the total POSAS score (the combined observer and patient scores) at 1 year between the 2 groups (16.69 ± 5.23 and 19.82 ± 6.53 , respectively, for the experimental and the control groups; P = 0.166; Fig. 3).







Fig. 3. POSAS total score.

	Control Group	Group Receiving Celergen	Р
Complications	4	9	0.99 (NS)
Seroma	2	4	1 (NS)
Hematoma	1	3	1 (NS)
Wound dehiscence	1	1	0.50 (NS)
Cellulitis	0	1	1 (NS)

Table 2. Postsurgery Complications

P: Student's *t* test.

NS, not significant.

Nine complications were reported in the group receiving supplementation (3 hematomas, 4 seromas, 1 dehisced wound, and 1 uncollected cellulitis), and 4 in the control group (2 seromas, 1 dehisced wound, and 1 hematoma). There was no significant difference between the 2 groups (Table 2).

DISCUSSION

Cutaneous wound healing is a complex process that can be considerably compromised by inadequate nutrition and protein deficiency. Wound healing in fact requires a great deal of collagen synthesis, and hypoproteinemia causes decreased fibroblast proliferation, reduced collagen synthesis, restricted angiogenesis, and altered collagen remodeling. For patients who have undergone bariatric surgery, whether the procedure was restrictive or malabsorptive, weight loss is often accompanied by inadequate nutrition after surgery.^{3,5,25–28} In our study, using a food supplement to complement the procedure appeared to improve the time to wound healing and the quality of the abdominoplasty scar.

Two studies have demonstrated the efficacy of Celergen for ultraviolet radiation-induced skin aging and for skin rejuvenation (elasticity, sebum production, significant increase in plasma hydroxyproline, and ATP storage in the erythrocytes).^{22,29} A third in vitro study showed improvement



Fig. 4. Patient in supplementation group, 1 year postsurgery: PO-SAS observer score: 11; POSAS patient score: 38.

in cellular wound healing in patients receiving Celergen compared with a control group by increasing fibroblast proliferation and migration, stimulating cell growth, increasing collagen production, and upregulating pro-collagen.¹⁹

Our study showed statistically significant improvement in time to wound healing in the group receiving supplementation compared with the control group (24.6 ± 9.31 and 34 ± 13.48 days, respectively; P=0.03), that is, the first day that scars no longer required dressing. These results were in line with our expectations. Indeed, it was proven that numerous patients who had achieved substantial weight loss (following lifestyle changes alone or after surgery) very often presented inadequate nutrition or malnourishment, and therefore exhibited slower cutaneous wound healing.^{7,28}

There was a significant difference in the experimental group and the control group POSAS observer score at 1 year (12.68 ± 6.6 and 17.38 ± 5.24 , respectively; P =(0.01). There appeared to be no difference in the POSAS patient score $(20.69 \pm 9.24 \text{ and } 22.25 \pm 7.82, \text{ respectively})$ and the POSAS total score $(16.69\pm5.23 \text{ and } 19.82\pm6.53)$, respectively; P = 0.166). An evaluation bias must however be noted. The POSAS is a subjective scale, with half the scoring coming from an observer, in this case a plastic surgeon who is accustomed to evaluating scars, and the other half the scoring coming from a patient who is inexperienced at giving this type of opinion. Some patients assess their scar poorly, and the discrepancy between the POSAS observer score and the POSAS patient score in some cases reached as much as 27 points (Figs. 4, 5). The differences between the POSAS observer score and patient score ranged from 0 to 28, but the POSAS patient score was never better than the POSAS observer score. Certain patients were dissatisfied because although the scar was covered by undergarments, it remained visible 1 year after the procedure.

The rate of minor complications observed in our patient group was 46% (6 seromas, 4 hematomas, 2 dehisced wounds, and 1 uncollected cellulitis). There were no other significant differences between the 2 groups (P = 0.99). Although this rate of minor complications is high, it corresponds to the figures appearing in the literature, which vary between 11.7% and 66%.^{7,30} No major complications were observed (thrombosis, pulmonary embolism).

Twelve patients underwent liposuction, including 9 in the group receiving supplementation (45%) and 3 in the control group (37.5%). Among the first group of patients, 5 complications were reported (3 seromas, 1 hematoma,



Fig. 5. Patient in supplementation group, 1 year postsurgery: POSAS observer score: 16; POSAS patient score: 17.

and 1 dehisced wound), and in the control group 1 complication was reported (1 hematoma). Various studies have looked at the relationship between liposuction performed during abdominoplasty and complications. In their retrospective study of 1,008 patients, Neaman et al.³¹ observed an increase in the number of seromas in the group that had both abdominoplasty and liposuction (P < 0.05). By contrast, in their study that enrolled 11,191 patients, Vieira et al.³² reported a decrease in the number of seromas (P =0.03) and other complications (P = 0.046) in the group that underwent liposuction and abdominoplasty, when compared with the group undergoing abdominoplasty alone.

In each group, 2 patients were smokers (P = 0.55). One of them in the control group suffered from a seroma complication. The other patient, who was in the group receiving supplementation, presented a hematoma. In their review with meta-analysis, Pluvy et al.³³ demonstrated that tobacco use exposes patients to an increased risk of cutaneous necrosis, delayed wound healing, and surgical-site infection in the event of major detachment among patients who smoke.

All our patients had previously undergone bariatric surgery (Table 1). They were therefore followed by a nutritionist who referred them to us for abdominoplasty once the deficiencies had been supplemented. No patient had poor nutrition or anemia.

Our study nevertheless had an important limitation. Because it involved only 28 patients, its statistical power was low. Nevertheless, this was a pilot study that produced promising results and it would be worthwhile to conduct a similar study with a broader scope.

CONCLUSIONS

As more and more patients undergo bariatric surgery, the number of patients who seek care to address the aftereffects of major weight loss is also increasing. These procedures result in large scars that cause functional, aesthetic, and psychological discomfort, which should not however constitute an obstacle to having the surgery performed.

Due to a rise in obesity and an increase in the number of bariatric surgery procedures, plastic surgeons are going to find that more and more patients suffer from the aftereffects of weight loss. The primary surgical procedure performed after bariatric surgery is abdominoplasty, which leaves a scar that is too often deemed to be unsightly. Oral treatments that may improve the scar appear to be beneficial.

All of these results show that Celergen supplementation is effective for patients undergoing abdominoplasty, with an impact on time to wound healing and the POSAS observer score at 1 year. Our study was nevertheless a pilot study with low statistical power, and it would be necessary to conduct a study with a broader-scope.

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REFERENCES

- OMS | Obésité et surpoids [Internet]. WHO. [cited 2017 Dec 12]. Available at http://www.who.int/mediacentre/factsheets/ fs311/fr/.
- 2. Santé publique France Etude ESTEBAN 2014–2016 Chapitre corpulence : stabilisation du surpoids et de l'obésité chez l'enfant et l'adulte [Internet]. [cited 2017 Dec 12]. Available at http://www.santepubliquefrance.fr/Actualites/Etude-ESTEBAN-2014-2016-Chapitre-corpulence-stabilisation-du-surpoids-et-de-lobesite-chez-l-enfant-et-l-adulte.
- Lupoli R, Lembo E, Saldalamacchia G, et al. Bariatric surgery and long-term nutritional issues. World J Diabetes. 2017;8:464–474.
- Ma C, Avenell A, Bolland M, et al. Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. *BMJ*. 2017;359:j4849.
- 5. Health Quality Ontario. Bariatric surgery: an evidence-based analysis. *Ont Health Technol Assess Ser.* 2005;5:1–148.
- Kitzinger HB, Abayev S, Pittermann A, et al. After massive weight loss: patients' expectations of body contouring surgery. *Obes Surg.* 2012;22:544–548.
- Albino FP, Koltz PF, Gusenoff JA. A comparative analysis and systematic review of the wound-healing milieu: implications for body contouring after massive weight loss. *Plast Reconstr Surg.* 2009;124:1675–1682.
- Staalesen T, Elander A, Strandell A, et al. A systematic review of outcomes of abdominoplasty. *JPlast Surg Hand Surg*. 2012;46:139– 144.
- Greco JA 3rd, Castaldo ET, Nanney LB, et al. The effect of weight loss surgery and body mass index on wound complications after abdominal contouring operations. *Ann Plast Surg*. 2008;61:235–242.
- Austin RE, Lista F, Khan A, et al. The impact of protein nutritional supplementation for massive weight loss patients undergoing abdominoplasty. *Aesthet Surg J.* 2016;36:204–210.
- Naghshineh N, O'Brien Coon D, McTigue K, et al. Nutritional assessment of bariatric surgery patients presenting for plastic surgery: a prospective analysis. *Plast Reconstr Surg.* 2010;126:602–610.
- 12. Russell L. The importance of patients' nutritional status in wound healing. Br J Nurs Mark Allen Publ. 2001;10:42–49.
- Heyman H, Van De Looverbosch DE, Meijer EP, et al. Benefits of an oral nutritional supplement on pressure ulcer healing in long-term care residents. *J Wound Care.* 2008;17:476–8, 480.
- Leigh B, Desneves K, Rafferty J, et al. The effect of different doses of an arginine-containing supplement on the healing of pressure ulcers. *J Wound Care.* 2012;21:150–156.
- 15. Sipahi S, Gungor O, Gunduz M, et al. The effect of oral supplementation with a combination of beta-hydroxy-betamethylbutyrate, arginine and glutamine on wound healing: a retrospective analysis of diabetic haemodialysis patients. *BMC Nephrol.* 2013;14:8.
- Bauer JD, Isenring E, Waterhouse M. The effectiveness of a specialised oral nutrition supplement on outcomes in patients with chronic wounds: a pragmatic randomised study. *J Hum Nutr Diet*. 2013;26:452–458.
- 17. Badr G. Camel whey protein enhances diabetic wound healing in a streptozotocin-induced diabetic mouse model: the critical role of β-Defensin-1, -2 and -3. *Lipids Health Dis.* 2013;12:46.
- Badr G, Badr BM, Mahmoud MH, et al. Treatment of diabetic mice with undenatured whey protein accelerates the wound healing process by enhancing the expression of MIP-1α, MIP-2, KC, CX3CL1 and TGF-β in wounded tissue. *BMC Immunol.* 2012;13:32.
- 19. A marine neutraceutica promotes fibroblasts proliferation, migration and collagen synthesis in damaged cells: an in vitro study revisiting the concept of "cell therapy"? Available at http:// monteiro-consulting.es/wp-content/uploads/Celergen-Text-Belletti.pdf.

- van Neerven SG, Krings L, Haastert-Talini K, et al. Human Schwann cells seeded on a novel collagen-based microstructured nerve guide survive, proliferate, and modify neurite outgrowth. *Biomed Res Int.* 2014;2014:493823.
- Han X, Zhang W, Gu J, et al. Accelerated postero-lateral spinal fusion by collagen scaffolds modified with engineered collagenbinding human bone morphogenetic protein-2 in rats. *PLoS One*. 2014;9:e98480.
- Marotta F, Kumari A, Yadav H, et al. Biomarine extracts significantly protect from ultraviolet A-induced skin photoaging: an ex vivo study. *Rejuvenation Res.* 2012;15:157–160.
- van der Wal MB, Tuinebreijer WE, Bloemen MC, et al. Rasch analysis of the Patient and Observer Scar Assessment Scale (POSAS) in burn scars. *Qual Life Res.* 2012;21:13–23.
- Vercelli S, Ferriero G, Sartorio F, et al. How to assess postsurgical scars: a review of outcome measures. *Disabil Rehabil.* 2009;31:2055–2063.
- Gantwerker EA, Hom DB. Skin: histology and physiology of wound healing. *Facial Plast Surg Clin North Am.* 2011;19:441–453.
- Agha-Mohammadi S, Hurwitz DJ. Potential impacts of nutritional deficiency of postbariatric patients on body contouring surgery. *Plast Reconstr Surg.* 2008;122:1901–1914.

- Bal BS, Finelli FC, Shope TR, et al. Nutritional deficiencies after bariatric surgery. *Nat Rev Endocrinol.* 2012;8:544–556.
- Agha-Mohammadi S, Hurwitz DJ. Nutritional deficiency of postbariatric surgery body contouring patients: what every plastic surgeon should know. *Plast Reconstr Surg.* 2008;122:604–613.
- 29. De Luca C, Mikhal'chik EV, Suprun MV, et al. Skin antiageing and systemic redox effects of supplementation with marine collagen peptides and plant-derived antioxidants: a single-blind case-control clinical study [Internet]. *Oxid Med Cell Longev.* 2016. Available at https://www.hindawi.com/journals/omcl/2016/4389410/.
- Hasanbegovic E, Sørensen JA. Complications following body contouring surgery after massive weight loss: a meta-analysis. J Plast Reconstr Aesthet Surg. 2014;67:295–301.
- Neaman KC, Armstrong SD, Baca ME, et al. Outcomes of traditional cosmetic abdominoplasty in a community setting: a retrospective analysis of 1008 patients. *Plast Reconstr Surg.* 2013;131:403e–410e.
- Vieira BL, Chow I, Sinno S, et al. Is there a limit? A risk assessment model of liposuction and lipoaspirate volume on complications in abdominoplasty. *Plast Reconstr Surg.* 2018;141:892–901.
- Pluvy I, Panouillères M, Garrido I, et al. Smoking and plastic surgery, part II. Clinical implications: a systematic review with metaanalysis. *Ann Chir Plast Esthet*. 2015;60:e15–e49.