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Review

Metabolic changes after nonsurgical fat removal: A dose response meta-analysis

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Lipid profile

Summary *Background:* Obesity-induced insulin resistance leads to the metabolic syndrome. Both bariatric surgery and surgical fat removal have been shown to improve metabolic health, but the metabolic benefits of nonsurgical fat removal remain uncertain. The aim of this paper is to establish whether nonsurgical fat removal exerts measurable, lasting metabolic benefits by way of changes to serum lipid profiles.

Methods: PubMed, Cochrane CENTRAL, Embase, and clinical trials registers were searched using the Polyglot Search Translator to find studies examining quantitative changes in metabolic markers after nonsurgical body contouring procedures. The MethodologicAl STandard for Epidemiological Research (MASTER) scale was adopted for the quality assessment of the included studies. The robust-error meta-regression (REMR) model was employed.

Results: Twenty-two studies and 676 participants were included. Peak body compositions measures manifest as a reduction of 2 units in body mass index (BMI), 1 kg of body weight (BW), 5 cm in waist circumference (WC) and 1.5 cm in abdominal fat thickness (FT), sustained up to 60 days postprocedure. Transient increases of 15 mg/dL in low-density lipoprotein (LDL), 10 mg/dl in triglycerides (TG), and 15 mg/dl in total cholesterol (TC) were observed at 2 weeks postprocedure.

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Conclusion: While nonsurgical fat removal exerts sustained effects on body anthropometrics, changes to serum lipid profiles were transient. There is no compelling evidence at present to support the conclusion that nonsurgical fat removal is metabolically beneficial.

Contents

Introduction

Obesity is a global health crisis and one of the principle causes of avoidable death in the developed world.[1] Chronic nutritional over sufficiency leads to adipocyte stress, upregulation of pro-inflammatory cytokines, recruitment of resident tissue macrophages, and, ultimately, local and systemic inflammatory dysregulation.[2] This pathophysiologic process exerts deleterious effects on insulin signal transduction[3] and is the crucial component of the metabolic syndrome.[4] Complications of the metabolic syndrome include atherosclerosis, hypertension, ischemic heart disease, liver disease, cancer, and susceptibility to respiratory infections, all of which have a basis in a common pathway of immune dysregulation.[5] There is some evidence to suggest that visceral fat is a key source of the cytokines (adipokines) that, collectively, induce insulin resistance.[6]

Reducing fat deposits through diet and exercise or by way of bariatric/metabolic surgery has observable, long-term immunologic and metabolic benefits.[7] More recently, it has been established that benefical effects can also be observed following surgical removal of subcutaneous fat by way of percutaneous avulsion and aspiration (liposuction) or by body contouring surgery such as abdominoplasty, belt lipectomy, brachioplasty, and bilateral breast reduction.[8,9] While these observations have not provided evidence of a magnitude or longevity of effect comparable with bariatric surgery, they have helped dispel the myth that body contouring surgery is merely an esthetic endeavor.

Nonsurgical fat removal is one of the fastest areas of growth and innovation within the aesthetics industry. Options include cryolipolysis, laser lipolysis, radiofrequency ablation, and high intensity focused thermal ultrasound (HIFU). While the mechanism of action of each method differs, the result is the focused elimination of subcutaneous fat in a noninvasive manner. The question of whether nonsurgical fat removal (NSFR) exerts measurable, beneficial metabolic benefits remains unclear. To answer this question, the current paper describes a systematic review and dose-response meta-analysis (DRMA) of observational studies pertaining to the metabolic impact of NSFR.

Methods

Search strategy

A search string was designed using relevant MeSH terms in PubMed, Cochrane CENTRAL, Embase databases, and online clinical trials registers using the Polyglot Search Translator.[10] The search strategy and used strings were designed and conducted by the first author (SB) and an experienced information specialist (JC) and were run across all databases on the 10th of March 2022. The search string included both medical subject heading (MeSH) terms and free-text terms. The online trial registers were searched at *ClinicalTrials.gov* and the national research registers were examined as well for relevant trials relating to nonsurgical body contouring procedures targeting the abdominal area and body compositions, and physiological and/or metabolic changes.

The Cochrane Highly Sensitive Search Strategy guideline in the Cochrane Handbook for Systematic Reviews of Interventions was adopted during the search process.[11] The results were reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Full search strings for all databases and the PRISMA checklist are available in **Supplementary Figures 1 and 2**.

Inclusion criteria

Papers and trials were included if they provided quantitative data permitting analyses of the effect of nonsurgical body contouring procedures (Ultrasound, cryolipolysis, radiofrequency, and high intensity electromagnetic) on body compositions, physiology, and/or metabolism. Only human studies that target the abdominal areas were considered. No search restrictions for a date, language, or publication were applied.

Exclusion criteria

Nonhuman (*in vivo*) studies were excluded from consideration as were studies that targeted other anatomical areas (e.g., thighs and arms) and studies on surgical body contouring procedures (e.g., abdominoplasty).

Quality assessment

The quality assessment of the eligibly included articles was independently done by two reviewers (SB and NJ) utilizing the MethodologicAl STandard for Epidemiological Research (MASTER) scale.[12] This scale evaluates each included study against 36 safeguards across seven domains that, if present, may mitigate systematic error in the trial. The MASTER scale delivered a robust framework for assessing the methodological quality of the included quasi-experimental and randomized controlled trials in this paper.

Outcome measures

The outcome measures sought include two domains. These included body compositions/ anthropometrics and lipid profiles. Data units were unified to the Systeme International d'Unites (SI) units. The extracted quantitative data (before and after nonsurgical body contouring procedures) included the following markers:

1. Body compositions/ anthropometric: BMI, BW, WC, and abdominal FT.
2. Lipid profile: LDL, high-density lipoprotein (HDL), TG, and TC.

Other body measurements and physiological/metabolic variables that were reported in less than 5 studies were excluded such as other anthropometrics measurements (e.g., hip circumference), fasting glucose, fasting insulin, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), leptin, fatty acids, C-reactive protein, very-low density lipoprotein (VLDL), alanine aminotransferase (AST), and aspartate aminotransferase (ALT).

Data extraction

Studies screening and data collection were retrieved from all full-text articles by four authors (SB, SI, GA, and NJ). Where necessary, clarification was sought with the senior author (GG).

Statistical methods

An "average" dose-response relationship between the measured outcome parameters (body compositions and lipid profile) and time elapsed after the body contouring procedure was established using the robust-error meta-regression (REMR) model.[13] Which represents a one-stage approach that treats each study as a cluster. The robust error variance was used in order to address any possible correlations among the within-study effects because these effects share the same reference within the single study. A nonlinear curve was fitted using restricted cubic splines with three knots. The Wald test was used to test for potential nonlinearity by assuming the coefficient of the nonlinear terms was zero. All analyses were performed using the *remr* module in Stata version 15, College Station, TX, USA.

Results

The conducted literature review resulted in a total of 818 articles and 33 registered trials (a total of 851 studies). Duplicate studies (252 studies) were excluded leaving 599 studies, of which 534 were excluded by title and abstract. The remaining 65 studies were examined by manuscript, and 46 studies were excluded due to a lack of a clear statement of the metabolic changes magnitude and/or the precise time of assessment after surgery. Eventually, 19 studies with a total of 601 participants were selected as relevant to this synthesis.[14-32] The conduct of the literature review is summarized by the PRISMA flowchart in Figure 1.

Characteristics of included studies

Characteristics of the selected studies are summarized in Table 1 and include study identifier, country, design, number of participants (sample size), population demographics, preoperative (baseline) BMI, type of nonsurgical body contouring procedure (Ultrasound (HIFU), cryolipolysis, radiofrequency, and high intensity electromagnetic), outcome measures (BMI, BW, WC, FT, LDL, HDL, TG, and TC), and follow-up time points after surgery (in days).

Table 1 Characteristics of included studies.

Study number	Study identifier	Country/ Region	Study design	Number of subjects	Population demographics	Baseline BMI (kg/m2)	Procedure	Outcome measures	Follow up time points (days)
1	Brightman et al., 2009	USA	quasi-experiment	10	Age 28- 70 years, all females	NA	radiofrequency + laser	WC	0, 30, 90
2	Shek et al., 2009	China & Japan)	quasi-experiment	53	51 females and 2 males, age range 26 – 69 years	N/A	ultrasound	FT, WC	0, 30
3	Choi et al., 2018	Korea	quasi-experiment	24	21 females and 3 males, age 20 - 60 years	23.97 ± 2.64	radiofrequency	FT, WC	0, 28, 56
4	Shek et al., 2014	China	quasi-experiment	12	9 females and 3 males, age 27- 56 years	25.230 ± 2.0310	ultrasound (HIFU)	WC, WT	0, 28, 56, 84
5	Boisnic et al., 2014	France	quasi-experiment	21	all females, age 31- 59 years	N/A	radiofrequency	FT, WC, WT	0, 30, 90
6	Tonucci et al., 2014	Brazil	quasi-experiment	20	all females, ages 18-60 years	25.85 ± 4.07	ultrasound	BMI, TC, HDL, LDL, TG, WC, WT	0, 14
7	Katz et al., 2019	USA	quasi-experiment	33	age 21- 65 years	20.0 - 30.0	high intensity electromagnetic	FT	0, 30, 90
8	Hong et al., 2019	Korea	quasi-experiment	20	17 females, 3 males,	27.34 ± 6 1.82	ultrasound (HIFU)	FT	0, 28, 56
9	Fonsea et al., 2018	Brazil	quasi-experiment	31	Females, age 20-40 years	≥ 30.0	ultrasound	TC, HDL, LDL, TG	0, 10
10	Arabpour-Dahoue et al., 2019	Iran	RCT	25	50 females, age 35.32 ± 8.70 years, DM, hyperlipidemia	16.1 - 56.7	radiofrequency+ US	TC, HDL, LDL, TG	0, 1
11	Moreno-Moraga et al., 2007	Spain	quasi-experiment	10	22 females and 8male, age 18 – 62 years	N/A	ultrasound	WC	0, 1

(*continued on next page*)

Table 1 (*continued*)

Study number	Study identifier	Country/ Region	Study design	Number of subjects	Population demographics	Baseline BMI (kg/m2)	Procedure	Outcome measures	Follow up time points (days)
12	ELdesoky et al., 2015	Middle east	RCT	20	5 males and 15 females, age 34.1 ± 4.95 years	32.67± 0.91	ultrasound	BMI, FT, WC, WT	0, 60
13	ELdesoky et al., 2015	Middle east	RCT	20	6 males and 14 females, age 33.3 ± 5.33 years	32.4 ± 1.0	cryolipolysis	BMI, FT, WC, WT	0, 60
14	Katz et al., 2019	USA	quasi-experiment	33	mean age 40.8 years	20.0 to 30.0	high intensity electromagnetic	FT	0, 30, 90
15	Robinson et al., 2014	USA	quasi-experiment	118	males and females, median age: 45.2 years	24.7 ± 2.6	ultrasound	WT	0, 28, 56, 84
16	Solish et al., 2011	Canada	quasi-experiment	45	majority females, age 42 −44 years	25.0 - 27.0	ultrasound	WT	0, 28, 56, 84
17	Verner et al., 2021	Middle east	quasi-experiment	15	females, mean age 45.5 ± 5.0 years	≤26	ultrasound	WC	0, 7, 30, 84
18	Khedmatgozar et al., 2020	Iran	quasi-experiment	30	females, age 18-65	29.55 ± 3.08	cryolipolysis	BMI, WC, WT	0, 56
19	Khedmatgozar et al., 2020	Iran	quasi-experiment	30	females, age 18-65 years	30.43 ± 4.38	Ultrasound cavitation, cryolipolysis, and diet	BMI, WC, WT	0, 56
20	Dhillon et al., 2018	United Kingdom	quasi-experiment	20	17 females 3 males, mean age 37.6 ± 7.11 years	25.1 ± 3.80	ultrasound	WC	0, 90
21	Fritz et al., 2017	Germany	quasi-experiment	20	18 females, 2 males	25.78 ± 2.37	ultrasound	WT, WC	0, 30
22	Guth et al., 2017	Brazil	quasi-experiment	24	males, age 18- 59 years	≤ 30	ultrasound (HIFU)	TC, HDL, LDL, TG	0, 1
23	Fonseca et al., 2018	Brazil	quasi-experiment	31	Females, age 20-40 years	≥ 30.0	ultrasound	TC, HDL, LDL, TG	0, 10
24	Boisnic et al., 2014	France	quasi-experiment	21	age 31 −59 years	N/A	radiofrequency	FT, WC, WT	0, 30, 90

RCT; randomized controlled trial. *BMI;* body mass index. *FM*; fat mass. *LBM*; lean body mass. *WC;* waist circumference. *TNF-* α; tumor necrosis factor alpha. *CRP*; C - reactive protein. *IL6*; interleukin 6. *FBG*; fasting blood glucose. *HOMA-IR*; homeostatic model assessment for insulin resistance. *SBP*; systolic blood pressure. *DBP*; diastolic blood pressure. *LDL*; low-density lipoprotein cholesterol. *HDL*; high-density lipoprotein cholesterol. *TC*; total cholesterol. *FFA*; free fatty acids. *L*; liters. *NR*; not reported.

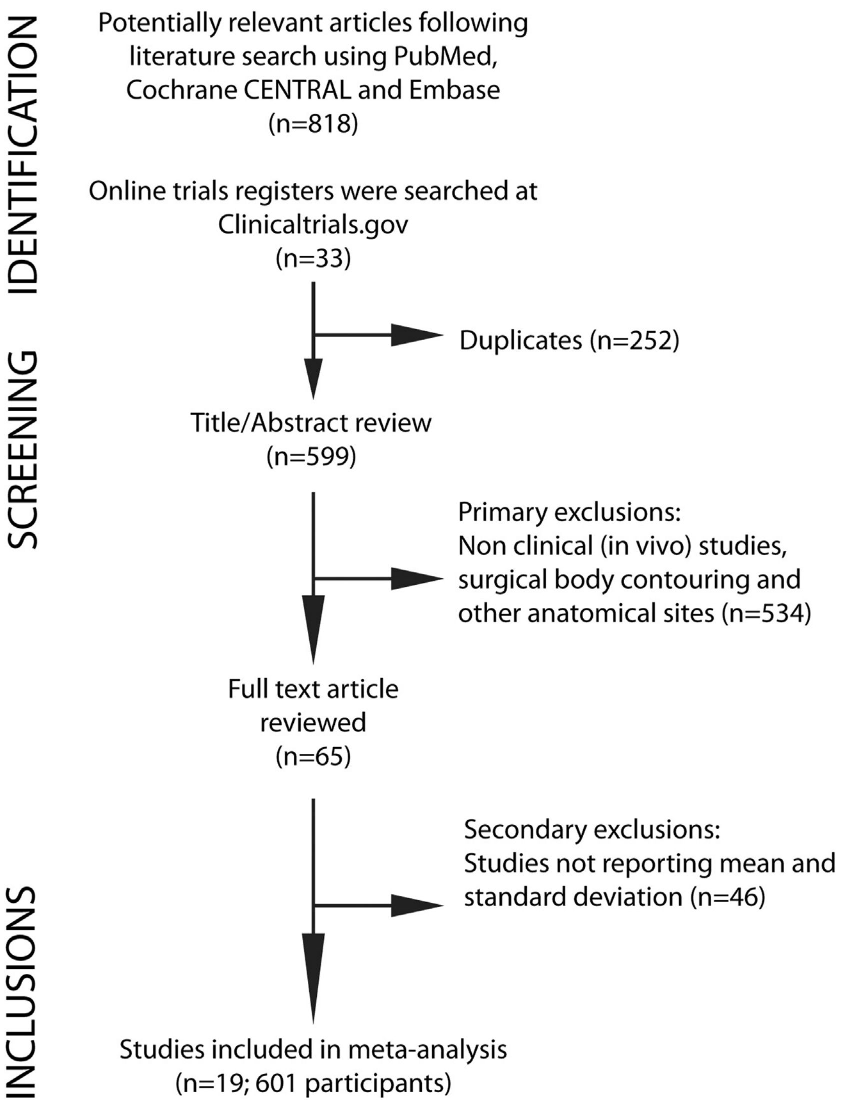

Figure 1 PRISMA flow diagram for selection of studies.

Metabolic changes after SFR

Anthropometrics / body compositions

Changes in (A) BMI, (B) BW, (C) WC, and (D) FT were measured over time in days since the body contouring procedure. A clear drop of 2 units in the BMI, 1 kg in the BW, 5 cm in WC, and 1.5 cm in abdominal FT was noted up to 60 days after the procedure. FT continued to decrease up to 90 days after the procedure. A moderate heterogeneity in the last three outcome variables was noted across studies, and the confidence intervals were wide due to the paucity of studies and the effect of bigger studies. However, the meta-analysis showed that the effect of body contouring procedures on BMI and related parameters persisted for at least 60 days. FT showed a clear continuous reduction up to 90 days after the procedure, see Figure 2**: A-D.**

Lipid profile

Changes in LDL, (B) HDL, (C) TG, and (D) TC were measured over time in days since the body contouring procedure. A serum increase of 15 mg/dL in LDL, 10 mg/dl in TG, and 15 mg/dl in TC was noted up to two weeks after the procedure. No significant change was noted in serum HDL. Due to the paucity of studies, confidence intervals were wide, and the trend could not be confirmed more precisely as this was driven by the bigger studies, see Figure 3**: A-D**.

Quality assessment of included studies

The majority of the included studies were ranked in the 4th quartile of the safeguards' count. Additionally, the most deficient safeguard standards were equal ascertainment and equal prognosis. On the other hand, the remaining standard safeguards were found to be less deficient. See **Supplementary Figure 3**.

Discussion

We examined the influence of nonsurgical body contouring procedures on body anthropometrics/ body composi-

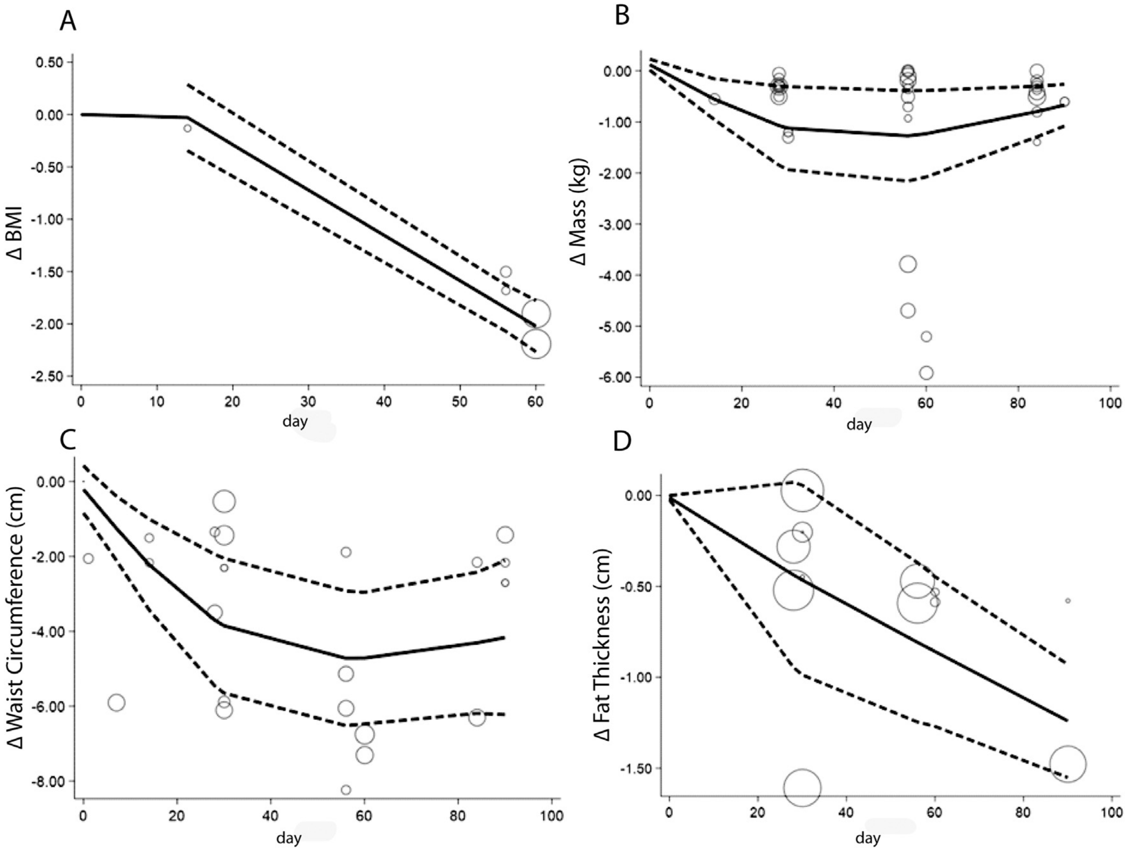

Figure 2 Change in (**A**) BMI, **(B)** BW, (**C**) WC, and **(D)** FT over time since body contouring procedure. The "dose" is time in days after the procedure. The circles represent the weighted mean difference in each individual study at this time point with the marker size reflecting the weight of corresponding study.

tion measurements and lipid profile using a systematic review of clinical data and subjected these data to a dose-response meta-analysis. Transient increases in serum LDLs, TG, and TC were observed up to two weeks following exposure to nonsurgical fat removal. In the longer term, no significant differences were observed. Anthropometric data confirmed a reduction in FT over the treated area, which persisted throughout the observation period (day 90). Taken as a whole, these data suggest that nonsurgical fat removal is efficacious, and that evidence of fat lysis may be inferred by transient rises in serum lipid profiles in the weeks following exposure to nonsurgical fat removal. However, no firm conclusions about the effect of nonsurgical fat removal on serum lipid profiles in the long term were permissible. This is in contrast to the results obtained when these analyses were performed for surgical fat removal. Here, the data confirmed that the surgical removal of fat by aspiration (liposuction) or excision (body contouring) resulted in favorable changes to the serum lipid profiles in the long term (Badran et al.- in press). Most likely, there were simply insufficient data to be able to conclude.

The preclinical and clinical evidence for favorable metabolic changes associated with cryolipolysis is variable. Using a porcine model, Kwon and colleagues[33] demonstrated that cryolipolysis was associated with a transient increase in serum TC, LDL and HDL cholesterol, and TG to day 30. By day 60, however, each had fallen below the baseline level. By day 90, serum LDL cholesterol was still below the baseline level. These observations were supported by a recently published study by Abdel-Aal et al.[34] involving 60 obese women randomized to receive a low-calorie diet for 3 months with or without 3 sessions of cryolipolysis. The group that received cryolipolysis demonstrated significant improvements in serum lipid profiles and liver enzymes relative to the control group. A study by Al Agamy et al.[35] comparing cryolipolysis with cold laser therapy observed a significant reduction in serum TG and a significant increase in serum HDL cholesterol following application of exposure to either device. This contrasts with the work of Klein and colleagues. In two separate studies of cryolipolysis of the flanks (40 patients)[36] and the abdomen and flanks (35 patients),[37] they reported no significant changes in serum lipid profiles over the timepoints studied. Similarly, a study of 50 patients by Ferraro et al.[38] exposed to cryolipolysis and extracorporeal shock wave therapy did not reveal any significant changes in serum lipid profile over 7 days. Clinical studies of lipolysis using high-intensity focused ultrasound (HIFU)[39,40] and radiofrequency failed to demonstrate significant changes in metabolic parameters after exposure. The transient nature of lipid profile variations observed in the current study was also observed in a preclinical study of laser lipolysis in pigs.[41]

The study raises several important questions about the role of nonsurgical fat removal as an endocrinological,

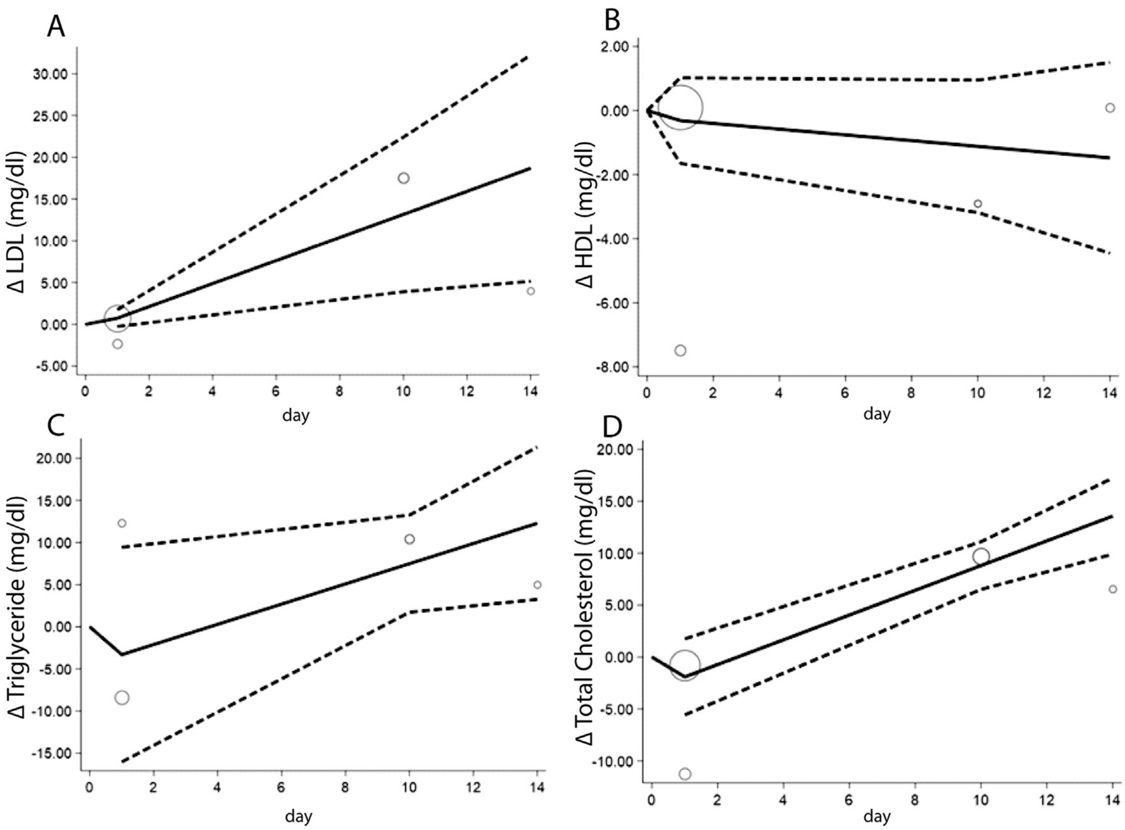

Figure 3 Change in (**A**) LDL, **(B**) HDL, (**C**) TG, and **(D)** TC over time since body contouring procedure The “dose” is time in days after the procedure. The circles represent the weighted mean difference in each individual study at this time point with the marker size reflecting the weight of corresponding study.

as opposed to purely esthetic, intervention. With a rising tide of obesity owing to calorie-rich diets and sedentary lifestyles, the desire for fat removal has fueled burgeoning surgical and nonsurgical aesthetics industries tailored to the pursuit of anthropometric ideals. Interestingly, however, these industries have neglected the potential health benefits of fat removal. Adipocytes regulate energy homeostasis by the synthesis and secretion of metabolic hormones known as adipokines.[3,5] It is hypothesized that circulating free fatty acids induce insulin-mediated triglyceride storage in adipose tissue, skeletal muscle, and liver. Chronic insulin overstimulation causes a stress response in each of these tissues with a synthesis of pro-inflammatory cytokines, recruitment of inflammatory cells, systemic inflammation, and insulin resistance via negative feedback controls. Many clinical studies have demonstrated that insulin sensitivity and lipid profiles may be improved merely by the removal of subcutaneous adipocytes.[42,43] It is interesting to speculate on whether evidence of metabolic benefits would influence the industry that has built up around nonsurgical fat removal. On the one hand, such evidence would be a powerful refutation of critics who espouse the view that there are no inherent health benefits to nonsurgical fat removal. On the other hand, more data are needed before authoritative conclusions can be reached.

A major limitation with this study is the small number of eligible studies, many of which had recruited a small number of patients. Thus, when the margin for error was taken into consideration, few obvious trends emerged. The lack of compelling source data reflects the fact that, on the whole, esthetic practitioners are less interested in the potential health benefits of nonsurgical fat removal than in the commercial potential of the pursuit of anthropometric ideals. If nothing else, this study highlights the pressing need for more metabolic data. Moreover, we included a number of different methods of nonsurgical fat removal. This inevitably leads to concerns that our data are heterogeneous and that, as such, our conclusions mean little for any one specific commercial device. The third limitation is the relatively limited number of metabolic parameters, and the narrow metabolic window studied. Again, we are limited by the data available from the source material.

Conclusion

This study shows that nonsurgical body contouring procedures correlates with a sustained improvement in anthropometrics and body compositions for at least two months after procedure. A transient deterioration in lipid profile is observed over the first two weeks, consistent with lipolysis. The long-term metabolic effects of nonsurgical fat removal remain uncertain.

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Category: Review.

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Ethical approval: Not required.

Declaration of Competing Interest

The authors declare no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2022.10.054.

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