Bariatric surgery: studies on its consequences with emphasis on thrombotic and bleeding complications

Çelik, F.

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No influence of weight loss after bariatric surgery on skin autofluorescence, a marker of advanced glycation end products

F. Celik, R. Graaff, M. Ahdi, E.W. Meesters, A.W.J.M. van de Laar, V.E.A. Gerdes

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ABSTRACT

Background:
Advanced glycation end products reflect cumulative glycemic stress and can be measured by skin autofluorescence (AF). Metabolic syndrome and adiposity are shown as independent predictors of advanced glycation end products accumulation.

Objective:
The objective of this study was to examine whether weight loss after bariatric surgery leads to a change of metabolic stress measured as skin autofluorescence.

Methods:
A total of 47 patients who had bariatric surgery were included. Skin autofluorescence, metabolic and clinical parameters were registered.

Results:
Mean age at the time of surgery was 41.2 ± 9.9 years. The mean follow up time between surgery and the second skin AF measurement was 26.9 ± 3.1 weeks. After surgery skin AF did not decrease: 1.99 AU (1.19 - 3.40) vs. 2.00 AU (1.27 - 3.21), while there were significant improvements for weight, BMI, waist circumference, pulse rate, C-reactive protein, HbA1c and cholesterol.

Conclusion:
In conclusion, skin AF remains high after bariatric surgery despite significant weight loss and improvement of metabolic and inflammatory parameters.

INTRODUCTION

The role of advanced glycation end products (AGEs) that reflect cumulative glycemic and inflammatory stress has been scientifically well accepted [1,2]. The accumulation of AGEs is increased with aging [3], diabetes [4,5], kidney disease [4], inflammation [5], but can also be derived from exogenous sources such as smoking [3]. Studies have shown strong associations between AGEs and complications of diabetes [4], cardiovascular disease [4], and mortality [4]. Metabolic syndrome and adiposity [6,7] are also shown as independent predictors of AGE accumulation. AGE measurements in skin biopsy and in serum have several drawbacks [2]. AGEs can also be measured noninvasively with an AGE Reader. The AGE Reader uses the fluorescent property of AGEs present in skin [2]. Because of the association of obesity with metabolic syndrome, diabetes and inflammatory stress [8], and the fact that weight loss leads to an improvement of these [9], we expect AGEs formation to be decreased. Since the AGE Reader measures the accumulation of AGEs, we were interested to investigate whether skin autofluorescence (AF) changes after the significant weight loss by bariatric surgery in (morbidly) obese patients.

MATERIALS AND METHODS

The prospective study was undertaken in morbidly obese patients who came to the outpatient clinic of internal medicine at the Slotervaart Hospital for the screening for bariatric surgery. A measurement of skin AF with the AGE Reader was performed before and six months after bariatric surgery during the regular visits. Because of a varying reflection coefficient (R) in different skin colors [2], only patients with a R>12% were included. Medical information was retrieved from the electronic patient files. Age at the time of the screening before surgery was registered. Type 2 diabetes was defined as an HbA1c ≥6.5% and/or use of antidiabetic drugs. Hypertension was defined as a blood pressure of above 140/90 mmHg and/or use of antihypertensive therapy. Dyslipidemia was defined as use of statins and/or a raised total cholesterol level, LDL or triglycerides above the 95st percentile according to the definition proposed by the American Heart Association [10]. Smoking was defined as current use of cigarettes. Blood pressure was measured using a Dinamap (automated Vital Signs Monitor, 300 series device, Welch Allyn Protocol Inc., Beaverton, Oregon USA). Blood pressure cuff size was chosen based on the circumference of the arm. AGE accumulation was assessed by measuring skin AF using the AGE Reader (Diagnoptics Technologies B.V. Groningen, the Netherlands) [3]. In short, the AGE Reader illuminates a

skin surface of approximately 4 cm^2, shielded from surrounding light, with an excitation light source between 300 and 420 nm (peak excitation ~370 nm) [3]. A series of three consecutive skin AF measurements were carried out at three positions at the volar side of the arm. In cases where the standard deviation of the triple measurement was above 12.5%, the median was calculated instead of the mean. Assuming that the mean skin AF in healthy Caucasian people is 1.81 ± 0.36 arbitrary units (AU) [3], we needed at least 36 patients to detect a difference of at least 0.2 AU to reach a power of 80% in paired analysis. Baseline characteristics of the patients were summarized. Comparisons of variables before and after surgery were made by Wilcoxon signed ranks test. Statistical analyses were performed using SPSS software (version 18.0).

RESULTS

A total of 47 patients who had bariatric surgery between February 2011 and September 2011 were included. Mean age at the time of surgery was 41.2 ± 9.9 years and 37 patients (79%) were female. 43 patients (91%) were Caucasian. Before surgery, diabetes was present in 8 (17%), hypertension in 16 (34%) and dyslipidemia in 16 (34%) patients. 9 patients (19%) were current smokers. The median weight of the group was 126.4 kg (99.6 - 164.0) and the BMI 43.7 kg/m2 (35.1 - 60.6). 46 patients (98%) had a laparoscopic gastric bypass surgery, and 1 (2%) a laparoscopic sleeve gastrectomy. The mean follow up time between surgery and the second skin AF measurement was 26.9 ± 3.1 weeks. After surgery skin AF did not decrease (before surgery 1.99 AU (1.19 AU - 3.40 AU) vs. 2.00 AU after surgery (1.27 AU - 3.21 AU)), while there were significant improvements for weight, BMI, waist circumference, pulse rate, C-reactive protein, HbA1c and cholesterol (figure 1). The mean weight and BMI loss after bariatric surgery were 29.6 kg (95% CI 12.9-46.3) and 10.1 kg/m2 (95% CI 4.7-15.6), respectively. Seven patients (15%) still smoked after surgery (p= 0.500).

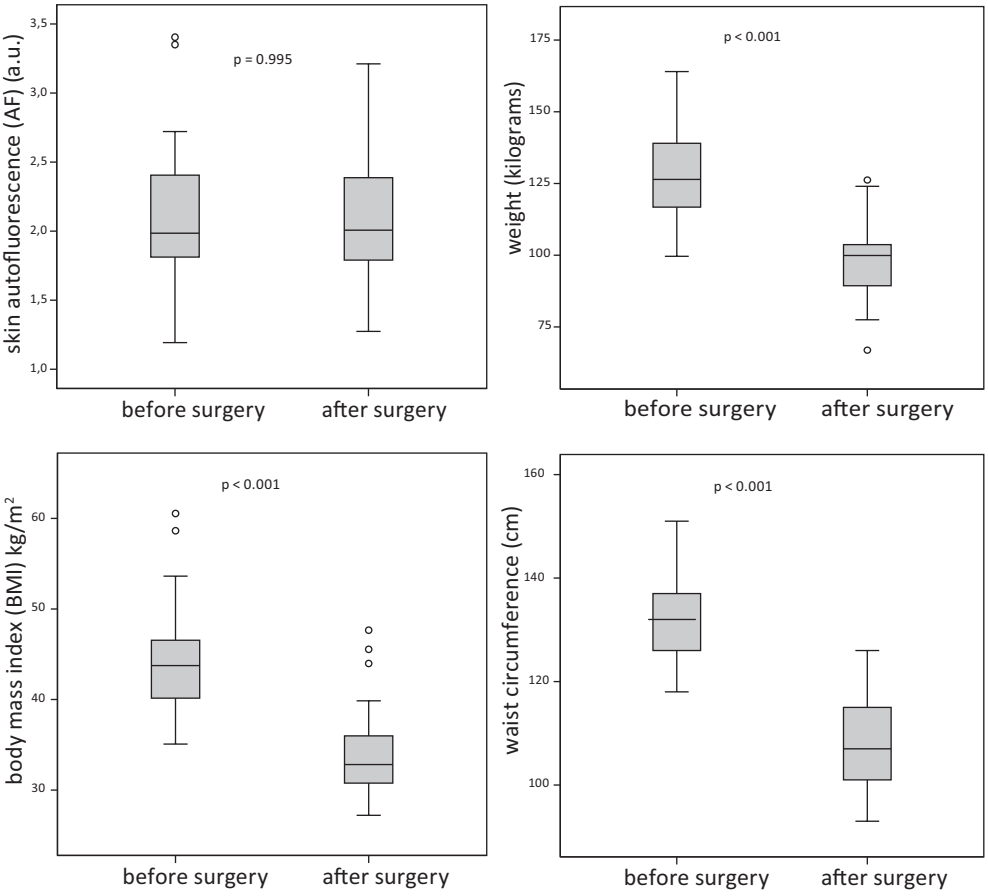

Figure 1. Changes of the parameters skin autofluorescence (AU), weight (kg), body mass index (kg/m^2), and waist circumference (cm) six months after bariatric surgery.

The Wilcoxon signed ranks test was used for all variables.

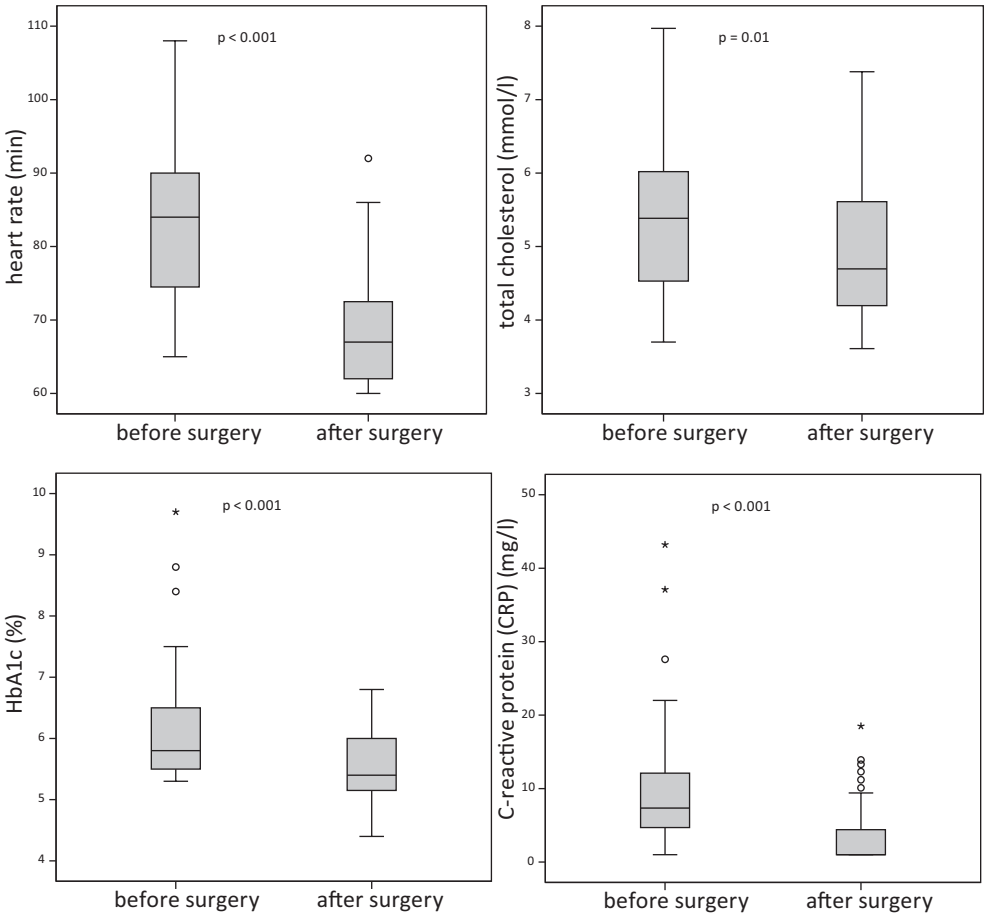

Figure 1. Continued.Changes of the parameters heart rate (min), total cholesterol (mmol/l), HbA1c (%) and C-reactive protein (mg/l) six months after bariatric surgery.

The Wilcoxon signed ranks test was used for all variables.

DISCUSSION

Previous studies showed that parameters of the metabolic syndrome and inflammation are increased in obese patients [8], and also improve in association with weight loss interventions [9]. In this study we could not detect an improvement in AGEs as determined by skin AF, while there were significant improvements for metabolic parameters. The effect of weight loss on skin AF has not been evaluated before to the best of our knowledge. Studies have shown that therapeutic interventions can inhibit the formation of AGEs for example with medication [11,12]. Other studies have shown that intensive treatment of hyperglycemia, as compared with conventional treatment, was associated with lower levels of glycation of skin collagen [13-15]. In the study of Graaff et al. [16], plasma AF reduced after a single haemodialysis session in patients with renal insufficiency, but there was no significant influence of the reduced plasma AF on skin AF.

There are several possible explanations for the maintenance of high skin AF after bariatric surgery in our study. First of all, skin AF is a measure of accumulated AGEs in skin. Skin collagen, for example, is a very long-lived protein and as a result AGE accumulation on these proteins reflect 'long term' metabolic stress [4,17]. The present results therefore suggest that changes in the actual value of the level of AGEs will not become visible from the measurement of skin AF. An important predictor of AGE accumulation is also smoking [4]. The fact that the number of patients who smoked after surgery did not change, may also contribute to the observation that skin AF did not decline. As the number of patients with diabetes was underrepresented in our cohort, it is possible that the study was underpowered. Furthermore, no specific attention was paid to potential errors for which some evidence has been provided, like food consumption that may influence the accumulation of AGEs [18]. Noordzij et al. [19] showed that AGE-rich meals may result in a postprandial rise in SAF. Furthermore, the AGE Reader has its own limitation. Fluorescent AGEs which are measured by the AGE Reader, are only a fraction of total AGEs. Non fluorescent AGEs are not measured with this tool. However, skin AF is correlated with levels of both fluorescent and nonfluorescent AGEs assessed in skin biopsies. Since we did not measure plasma AGEs, some decrease of AGEs in the plasma may have remained unnoticed.

CONCLUSION

In conclusion, AGEs as measured by skin AF remain high after bariatric surgery despite significant weight loss and improvement of metabolic parameters. Studies that include plasma AGEs as well are needed to clarify the contribution of different parameters to AGE formation and accumulation in obesity to get more insight in the possible link between weight change after bariatric surgery and the behavior of AGEs involving extended post surgical periods.

DISCLOSURE OF CONFLICT OF INTERESTS

R. Graaff is cofounder and stockholder of DiagnOptics Technologies B.V., the manufacturer of the AGE Reader™ (www.diagnoptics.com). No economical support was provided by any company.

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