SURGERY FOR OBESITY AND RELATED DISEASES

Surgery for Obesity and Related Diseases ▮ (2016) 00–00

Original article

Blunting of adaptive thermogenesis as a potential additional mechanism to promote weight loss after gastric bypass

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Received July 18, 2016; revised October 3, 2016; accepted November 17, 2016

Abstract

Background: Adaptive thermogenesis (AT) is described as a change in resting metabolic rate (RMR) that is greater than would be predicted from changes in lean body mass (LBM) and fat mass (FM) alone during periods of energy imbalance. Whereas an AT-related downregulation of RMR has been implicated in suboptimal weight loss and weight regain after nonsurgical weight loss, defense against AT may underpin the durable weight loss after laparoscopic Roux-en-Y gastric bypass (LRYGB) and other bariatric surgeries. However, methodological differences across the few studies that have evaluated postoperative AT limit interpretation as to the effects of these procedures on RMR.

Objective: To quantify AT 6 months after LRYGB and laparoscopic adjustable gastric banding (LAGB).

Setting: The study was conducted in a large university hospital in the United States.

Methods: Changes in body composition and RMR were assessed in 13 severely obese adults 6 months after LRYGB (n = 8) and LAGB (n = 5). AT was calculated as the difference between measured RMR and RMR predicted from LBM, FM, age, and sex before and after surgery.

Results: RMR significantly decreased after LRYGB (−270 ± 96 kcal/d, $P < .01$) but not after LAGB. Despite significantly greater reductions in weight, FM, and LBM with LRYGB than LAGB, AT responses after LRYGB (15 ± 110 kcal/d, $P = .7$) and LAGB (42 ± 97 kcal/d, $P = .4$) were similar ($P = .7$).

Conclusion: Despite significant weight and body composition changes, AT was minimal after Q4 LRYGB. A blunting of AT may be an additional mechanism that favors sustainable weight loss with LRYGB. (Surg Obes Relat Dis 2016;▮:00–00.) © 2016 American Society for Metabolic and Bariatric Surgery. All rights reserved.

Whereas diet and exercise can result in substantial short-term reductions in weight, consequential declines in energy expenditure challenge the ability of most individuals to lose significant amounts of weight over time [1–3]. Resting metabolic rate (RMR) accounts for most of the total daily energy expenditure, indicating the effect of lower metabolic costs of maintaining body tissues on post-weight loss energy balance. In comparison with the goal of optimizing the loss of fat mass (FM), the preservation of more thermogenic lean body mass (LBM) is often encouraged to attenuate the weight loss-related decrease in RMR. However, even intense strategies to spare LBM used in the popular weight loss series "The Biggest Loser" were incapable of preventing a significant decline in RMR [4]. Rather, reductions in RMR were greater than could be

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http://dx.doi.org/10.1016/j.soard.2016.11.016

explained by changes in weight and composition alone, as the regression equations that accurately predicted RMR from LBM and FM before the competition significantly overestimated RMR after weight loss [4–6]. This energy-sparing phenomenon was initially described as "adaptive thermogenesis" (AT) by Ancel Keys and his colleagues [7] over a half-century ago when they realized that participants in their landmark Minnesota Starvation Experiment found disproportionately large declines in RMR relative to the depletion of body cell mass after 6 months of severe caloric restriction. AT is now widely recognized as a dynamic counter-regulatory metabolic response that serves to mitigate changes in weight during periods of energy imbalance [7–10]. Recently, the effect of AT on weight loss outcomes received national attention (front page headline in *The New York Times*[11]) as "The Biggest Loser" participants were shown to have significant AT at 7 months after initial weight loss and that almost all participants had complete weight regain at 6 years of follow-up altogether with unexpected and persistent metabolic adaptation [6].

In contrast to nonsurgical interventions, current bariatric surgery techniques produce substantial and durable weight loss in most patients. Although these procedures result in significant reductions in both FM and LBM and, in turn, RMR, interestingly, some of the limited available evidence suggests that bariatric surgery may defend against energy-sparing with AT [5,10]. For instance, the 240 kcal/d greater decline in RMR observed after 7 months of participation in "The Biggest Loser" competition in comparison with 6 months after laparoscopic Roux-en-Y gastric bypass (LRYGB) was nearly entirely accounted for by a larger AT [5]. However, given the greater short- and long-term weight loss and body composition improvements with LRYGB in comparison with laparoscopic adjustable gastric banding (LAGB) [12], a separate finding that AT was significantly larger 6 months after LRYGB than LAGB [13] obscures understanding of how AT might affect post-operative energy balance.

Since AT is quantified as the difference between the measured change in RMR and that which would be predicted from changes in metabolically active tissues, differences in the study populations from which the pre-weight loss RMR prediction equations were developed (e.g., surgical and non-surgical weight loss seekers [5] versus surgical patients only [13]) and the independent variables included in the RMR prediction equations (e.g., LBM, FM, and age [5] versus LBM, age, and sex [13]) may have influenced the AT calculations in these studies. Therefore, the objective of this study was to quantify AT after LRYGB and LAGB by comparing measured RMR with RMR predicted from LBM, FM, age, and sex before and after surgery.

Methods

Thirteen participants (10 females) from our previously published study population [12] had complete anthropometric and RMR data both before and 6 months after bariatric surgery and thus constituted the subgroup used in this analysis. Eight participants elected to undergo LRYGB, and 5 elected to undergo LAGB. Eligibility criteria and assessment methods were previously described [12]. In short, body composition was assessed before and 6 months after surgery using dual x-ray absorptiometry (DXA, Hologics Discovery Wi, Bedford, MA, USA), and RMR was measured using open-circuit indirect calorimetry (SensorMedics, Deltatrac II Metabolic Monitor) after an overnight fast. Gas exchange measures were collected for at least 30 minutes with participants resting in the supine position, and the final 20 minutes of stable values were used to calculate RMR. All participants provided written consent before study participation. All procedures were approved by the University Committee on Human Research and General Hospital Clinical Research Center Advisory Committee.

Statistical analysis

We followed the methods of Knuth et al. [5] to predict preoperative RMR from LBM, FM, age, and sex using least squares linear regression. This same equation was then used to predict RMR 6 months after surgery. Differences between measured RMR ($RMR_{measured}$) and predicted RMR ($RMR_{predicted}$) were compared before and after surgery using independent *t* tests. AT was calculated using the established equation (6-month $RMR_{predicted}$ − baseline $RMR_{predicted}$) − (6-month $RMR_{measured}$ − baseline $RMR_{measured}$) [8]. A more positive value signified greater postoperative energy conservation due to AT, and a 1-sample means test was used to determine if AT reached statistical significance in comparison with zero (i.e., no difference between measured RMR and predicted RMR). Normality of all measures of interest was confirmed using Shapiro–Wilk tests. Thus, all values are presented as means and standard deviations. Baseline and 6-month differences in anthropometric and RMR measures were examined across all participants and within and between the LRYGB and LAGB groups using paired *t* tests.

Results

Patient demographic characteristics and weight, body composition, and RMR before and 6 months after bariatric surgery are presented in Table 1. Preoperative weight, body composition measures, and BMI did not differ between patients in the LRYGB and LAGB groups. LRYGB and LAGB each produced significant reductions in weight, LBM, and FM, whereas body fat percentage (BF%) decreased after LRYGB but not LAGB. RMR was significantly reduced after LRYGB only.

Adaptive thermogenesis

In the group as a whole, preoperative RMR was accurately predicted by the equation: RMR (kcal/d) =