The American Journal of Surgery xxx (2017) 1–4

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Exponential decay modeling can define parameters of weight loss trajectory after laparoscopic Roux-en-Y gastric bypass

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A R T I C L E I N F O

Article history:
Received 20 August 2017
Received in revised form
29 September 2017
Accepted 5 October 2017

Keywords:
Gastric bypass
Laparoscopy
Weight loss

A B S T R A C T

Background: Laparoscopic Roux-en-Y gastric bypass (LRYGB) produces durable and clinically significant weight loss. We aim to characterize the trajectory of weight loss, and demonstrate the predictive ability of three-month performance on final weight loss.
Methods: Retrospective analysis of 1097 consecutive LRYGB patients allowed for assessment of conformity of various weight loss trajectory models. Establishing exponential decay as the optimal fit, initial, three-month and final BMI values were used to determine empiric rate constants (λ_3). Empirically derived weight loss curves and associated rate constants (λ) were generated.
Results: Exponential decay optimally characterizes post-LRYGB weight loss trajectory. Final weight loss can be characterized by λ_3, as well as by the demographics black race ($P = 0.008$) and initial BMI ($P < 0.001$). Stratification by three-month weight loss allowed derivation of weight loss trajectory curves to predict weight at any point until and including plateau.
Conclusions: Weight loss after LRYGB conforms well to exponential decay, and postoperative trajectory can thus be predicted early. This allows the clinician early identification and intervention upon patients at risk of poor performance.

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1. Introduction

Over one-third of adults in the United States are considered obese, and this percentage continues to increase.[1] As the prevalence of obesity increases, so have obesity-related disorders, including type 2 diabetes mellitus, hyperlipidemia, hypertension, obstructive sleep apnea, heart disease, stroke, asthma, depression, and various malignancies.[1] Unfortunately, diet and lifestyle modifications are often ineffective in the long-term treatment of obesity.[2] Consequently, many patients undergo bariatric surgery for weight loss and amelioration of co-morbidities, as surgical intervention is regarded as the most effective, if not only sustained, treatment for morbid obesity and its sequelae. Weight loss varies among the type of bariatric surgery, and patients who have undergone Roux-en-Y gastric bypass (RYGB) have been shown to have the greatest amount of weight loss and comorbidity resolution compared to other techniques.[2–4] Following RYGB, the greatest amount of weight loss occurs in the first 6–12 months, and patients tend to plateau around 18 months postoperatively.[3,5,6]

Previous studies examining quantification of weight loss after RYGB have focused on fixed time points, without characterization of parameters of the weight loss trajectory.[3,5] While a handful of studies have attempted to characterize the trajectory of weight loss following RYGB, they have thus far proven algorithmically complex and have not translated to clinical utility.[2,3,7,8]

Variance in weight loss after bariatric surgery is governed in part by preoperative, intraoperative and postoperative factors related to the patient, surgeon, and institution. Among the multiple preoperative factors associated with long-term weight loss are age, initial body mass index (BMI) and diabetes.[9] After the operation, however, it is unclear whether weight loss at various intervals prior to a final, plateau value have predictive value for an ultimate weight loss. However, if short-term weight loss (e.g. three months postoperatively) can predict a final weight loss using a sound mathematical model, then perhaps the variance in final weight loss attributable to preoperative and intraoperative factors can be captured and manifest early in the postoperative period.

Currently, bariatricians use clinical experience and subjective interpretations of objective data to assess a patient's weight loss

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https://doi.org/10.1016/j.amjsurg.2017.10.024
0002-9610/Published by Elsevier Inc.

during postoperative follow-up visits. There lacks a clearly developed, simple model to characterize optimal weight loss trajectory following RYGB. To this effect, we aimed to derive an accurate and sufficiently facile model with which postoperative weight loss could be temporally characterized, while providing appropriate translation to clinical utility.

2. Methods

This was a retrospective cohort study performed using patients who underwent laparoscopic Roux-en-Y gastric bypass (LRYGB) at a single institution, Vanderbilt University Medical Center in Nashville, Tennessee. All patients were identified with, and information was gathered, using the Synthetic Derivative, a database mirroring StarPanel, the institutional electronic medical record. An algorithm is applied to all information within the Synthetic Derivative in which all identifying information is de-identified in accordance with the Health Insurance Portability and Accountability Act; as such, informed consent was waived after approval by the Vanderbilt University Institutional Review Board.[10]

The first objective of this investigation was to find a reasonably simple function to which postoperative weight loss had optimal conformity, from a panel of functions rationally determined *a priori*. The initial LRYGB cohort of 1762 was determined by query of the Synthetic Derivative for all patients having undergone LRYGB via directed *Current Procedural Terminology* code search (43644, Laparoscopy, surgical, gastric restrictive procedure with gastric bypass and Roux-en-Y gastroenterostomy [roux limb 150 cm of less]).[11] All postoperative BMI values for these patients, along with the postoperative day obtained, were recorded out to three years postoperatively. To best characterize a weight loss function, patients were required to have an initial BMI (BMI_0), as well as at least one value in each of three periods of time postoperatively: within 90 days, between 90 days and one year, and after one year.

To generate the optimal weight loss function, all postoperative BMI values were converted to %excess BMI remaining[12] (%EBMIR), defined as *100%(1- [BMI_0-BMI_t]/[BMI_0-25 kg/m^2])*. The first BMI value recorded in each of nine discrete postoperative time periods: 14–30 days, 31–60 days, 61–90 days, 91–180 days, 181–270 days, 271–365 days, 366–545 days, 546–720 days and 2–3 years, was taken, along with the postoperative day the value was obtained. All data points within each time period were averaged and plotted, with appropriate error bars reflecting the standard deviation of the %EBMIR displayed as a measure of dispersion. Simple models fit to the weight loss curve included exponential decay, quadratic and cubic regression. Goodness of fit was characterized by the Pearson r^2 value of the regression line. Ultimately proving the best fit function, one-phase exponential decay is represented by a function of the form

$$\%EBMIR_t = (100\%)\% \, e^{-\lambda t} + \%EBMIR_f$$

where $\%EBMIR_t$ is the percentage of excess BMI (over 25 kg/m^2) remaining at a given postoperative day *t*, 100% represents the excess BMI remaining at the time of surgery, $\%EBMIR_f$ represents the plateau percentage of excess BMI remaining and λ represents the exponential decay rate constant.

The second objective of the investigation sought to demonstrate the predictive ability of three month performance on ultimate weight loss, via lambda (λ) as a rate constant established at the three-month postoperative visit (λ_3). The cohort for this analysis was derived from the initial 1097 patients and excluded patients without a three month follow-up BMI (defined as between 61 and 90 days postoperatively [$BMI_{61\text{-}90}$]), as well as a BMI at 2–3 years postoperatively (taken as a surrogate of final BMI [BMI_f]). In this analysis, BMI_0, $BMI_{61\text{-}90}$ and BMI_f were used to solve for λ_3, nonetheless, we sought to demonstrate an independent association of λ_3 with $\%EBMIR_f$. Demographics including gender, race, age and BMI_0 were assessed for association with λ_3 on bivariate and subsequent standard least squares multiple linear regression analysis, to preclude their inclusion in the subsequent analysis of the association of λ_3 and $\%EBMIR_f$. Analogous analysis was done to determine those factors, including λ_3, associated with $\%EBMIR_f$. Finally, a multivariate linear regression model was developed and plotted, including all variables independently associated with $\%EBMIR_f$. A criterion of $P < 0.05$ was used to denote statistical significance.

The final objective was to use the concept of individual rate constants to translate the model into a clinically useful representation of exponential decay. To do this, pictorial depictions of exponential decay to be assigned at the three month follow-up encounter were derived. All data points from the 653 patients who had a three month follow-up visit available were assessed. Patients were stratified based on their three month performance, and average growth curves were generated from exponential decay regressions of their subsequent weight loss performance.

3. Results

Within the 1097 patient cohort, 22.6% of the patients were male gender and 16.0% were black race, while the mean age and BMI_0 were 46.9 years and 48.4 kg/m^2, respectively. Mean BMI_f was 31.6 kg/m^2. Determination of the best-fit simple weight loss function is illustrated in Fig. 1, which reveals the superiority of one-phase exponential decay to two representative alternative functions: quadratic and cubic regression. Pearson r^2 values of the exponential decay, quadratic and cubic models were 0.72, 0.68 and 0.71, respectively. The exponential decay curve depicted in Fig. 1 was further characterized by a $\lambda = 7.5 \times 10^{-3}$ and a $t_{1/2}$ (time to achieve half of the ultimate weight loss) = 93 days.

Upon bivariate linear regression analysis, both male gender ($P < 0.001$) and age ($P = 0.02$) were associated with λ_3. Black race ($P = 0.15$) and BMI_0 ($P = 0.15$) were not associated with λ_3. Upon multivariable analysis considering gender and age, both demonstrated an independent association with λ_3, with respective *P* values of < 0.001 and 0.046. To demonstrate the independent association of λ_3 with $\%EBMIR_f$, initial bivariate analysis of male gender, black race, age and BMI_0, as well as λ_3 was performed, demonstrating a significant association of all variables. On subsequent multivariable analysis, black race ($P = 0.008$), BMI_0 ($P < 0.001$) and λ_3 ($P < 0.001$) were independently associated with $\%EBMIR_f$. The multivariable analysis was re-performed without inclusion of gender and age, whose influence on the outcome was contained within the λ_3 variable. Black race ($P = 0.01$), BMI_0 ($P < 0.001$) and λ_3 ($P < 0.001$) all remained independently associated with $\%EBMIR_f$. Actual $\%EBMIR_f$ values were plotted against those predicted by the multivariable model which considered λ_3, race and BMI_0. Illustrated in Fig. 2, there was high correlation with a Pearson r^2 value of 0.68.

The 653 patients with 3 month follow-up visits were stratified by three month performance. Strata included <0.25% excess body-mass index loss (EBMIL)/day (d), 0.25–0.30% EBMIL/day, 0.30–0.35% EBMIL/d, 0.35–0.40% EBMIL/d, 0.40–0.45% EBMIL/d, 0.45–0.50% EBMIL/d, 0.50–0.60% EBMIL/d and >0.60% EBMIL/d. Taking averages of data points of all patients within each strata, empiric exponential decay curves were plotted and a lambda was generated. These curves, which can be assigned to patients at their three month follow-up, are illustrated in Fig. 3.