Biexponential Model for Predicting Weight Loss after Gastric Surgery for Obesity

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Submitted for publication May 2, 2001

Background. Following gastric restrictive surgery, morbidly obese patients rarely achieve their ideal body weight defined by Metropolitan Life tables. The final body weight will depend on the initial body composition because there will be greater weight loss from fat than lean body mass. The purpose of this study was to develop a mathematical model that accurately estimates the rate and extent of weight loss following gastric bypass surgery.

Methods. Patients underwent gastric bypass followed by intensive medical therapy and serial bioelectrical impedance analysis (BIA) body composition measurements. Differential equations were derived to model weight loss.

Results. Weight loss in the fat and lean body compartments followed monoexponential decay kinetics with differing rate constants. Total body weight loss \( W_T \) at time \( t \) was

\[
W_T = \frac{k_f}{(k_f - k_l)} \left( W_{lo} e^{-k_l t} + W_{fo} e^{-k_f t} \right),
\]

where \( W_{fo} \) and \( W_{lo} \) are the initial fat and lean body masses determined by BIA and \( k_f \) and \( k_l \) are the rate constants for the fat and lean compartments, respectively. Following surgically induced weight loss, \( k_f = 7.61 \pm 1.27 \times 10^{-2} \) and \( k_l = -0.93 \pm 0.13 \times 10^{-2} \), with the ratio of residual sum of the squares to the total sum of the squares of 98.8%.

Conclusion. Accurate prediction of weight loss depends on the initial fat and lean compartment mass since each of these loses weight at a different rate and to a different extent. When these effects are accounted for, the total body weight loss can be accurately predicted for any given time following surgery.

Key Words: compartment modeling; biexponential models; obesity surgery; gastric bypass; weight loss; mathematical models; bioimpedance analysis.

INTRODUCTION

Morbid obesity is a serious disease with multiple medical and psychological complications [1, 2]. When nonsurgical methods fail to achieve or maintain a significantly reduced body weight, bariatric surgery becomes a viable option. Surgery is very effective in treating obesity-related comorbid conditions such as hypertension [3], diabetes [4, 5], dyslipoproteinemia [6–8], sleep apnea [9–11], and pulmonary hypertension [12, 13]. Although the primary reason to perform antiobesity operations is to ameliorate these health problems, patients and physicians alike view weight loss goals in terms of target weights.

The most commonly used target weights are obtained from published weight-for-height tables [14]. These tables establish ideal weights for a given height, based on the lowest mortality observed with longitudinal follow-up. Most studies of bariatric operations have used life tables for determination of the ideal body weight and expressed the final weight in terms of excess weight loss relative to the ideal weight found in the tables. In general, for gastroplasty, the typical weight loss is expected to be 40% of excess weight and for gastric bypass, about 60% [15]. Use of height/weight tables has resulted in the perception that the ideal weight is not achieved. Relying on ideal body weight also fails to account for changed body composition, namely that of fat versus lean tissue mass [16]. Unre-
alistically low target weights might result in excessive loss of lean body mass. Failure to achieve the low target weight leads to patient frustration and resultant dissatisfaction with surgery [17].

Obese individuals have heterogeneous body compositions. A relatively small muscle mass and a high proportion of fat characterize sarcopenic obesity. Hypermuscular individuals have a very large muscle mass with proportionately less fat. There is differential weight loss from the fat and muscular compartments: fat is lost rapidly and muscle mass more slowly. Total body lean and fat mass are reasonably estimated with bioelectrical impedance analysis (BIA), a noninvasive and reproducible technique for assessing body composition. The correlation between body composition determination by BIA and other standard techniques is very good [18, 19]. Using this methodology we monitored fat and lean body mass loss following obesity surgery. From this we developed a biexponential model predicting weight loss that accounted for the differential weight loss observed from the fat and lean body compartments. This facilitated establishment of realistic target weights for postoperative gastric bypass patients.

**METHODS**

Prior to accepting patients for surgery, a multidisciplinary team consisting of surgeons and internists specializing in clinical nutrition evaluated all patients. A specialist in pulmonary/critical care evaluated patients with sleep apnea, respiratory disease, or multiple medical problems. Patients were considered for surgery only if they met surgical criteria as outlined in the National Institutes of Health consensus statement regarding obesity surgery [15, 20]. Surgery was offered only if all team members agreed that surgery was appropriate for the patient.

We prospectively evaluated BIA for preoperative determination of target weight in a series of 28 patients undergoing Roux-en-Y gastric bypass (RYGB) for morbid obesity. Body composition measurements were taken immediately before surgery and in the range of 4–18 months following surgery. A secondary phone and/or mail survey was taken 22–50 months following surgery, requesting the patient’s current weight and status of preoperative comorbid conditions.

Each patient had height and weight measured. Bioimpedance measurements were obtained as outlined below. Patients were followed weekly for 1 month prior to surgery, during which time they received nutritional counseling and were started on a diet program. During this time, compliance with dietary and follow-up instructions further assessed a patient’s suitability for surgery.

Body composition measurements. Weight was measured with a doctor’s scale calibrated to the nearest 0.25 lb and height was measured with a wall-mounted stadiometer to the nearest 0.25 in. Body mass index (BMI) was calculated by dividing the weight (kg) by the height squared (m²). Subjects underwent BIA with a tetrapolar bioimpedance meter programmed to estimate fat-free mass and fat mass with regression equations based on data obtained by comparing bioimpedance estimates with hydrodensitometry (Space Labs BC-300 Body Composition Analyzer, Biodynamics, Inc., Bellingham, WA). BIA measures electrical impedance that varies in proportion to fat-free mass. Obesity is associated with overhydration that affects BIA estimates of lean body mass [21]. The BC-300 accounts for this by selecting different fat-free mass–estimating equations based on body habitus and sex.

Total body resistance was measured in the supine position. Two electrodes were placed on the dorsal surface of the right hand and foot just proximal to the metacarpal and metatarsal phalangeal joints, respectively. The other two electrodes were placed on the dorsal surface of the wrist at the level of the ulnar tubercle and on the dorsal surface of the foot between the lateral and medial malleoli [22].

Surgery. All patients received at-home bowel preparation and were admitted the day of surgery. A standard RYGB was performed: an ETHICON TA-60 heavy wire stapler was fired obliquely across the stomach, creating a 30-cc proximal gastric pouch. The jejunum was divided 30 cm distal to the ligament of Treitz, and the first arcade of mesenteric vessels was divided with a vascular gastrectinal anastomosis stapler. The distal cut end of the jejunum was then tunneled through the transverse mesocolon to lie anterior to the stomach. It was anastomosed to the pouch side to side with a single layer of 3-0 Maxon suture over a 32-French bougie catheter, creating a 1-cm anastomosis. The procedure was completed by performing a side-to-side jejunojejunostomy 40 cm distal to the gastrojejunalostomy.

Postoperative care. On postoperative day 2, patients were routinely started on a special liquid diet (stage I diet). Fluid intake was restricted to less than 3 fluid ounces per hour and consisted of Ultra Slim-Fast, clear fruit juices (apple, grape, or cranberry) diluted 50/50 with water, vegetable or chicken broth, decaconated (flat) diet soda, or diet j ell-O. Patients remained on this liquid diet for 3 weeks postoperatively. The stage I diet restricted fluid intake to less than 8 ounces per hour and was initiated 3 weeks following surgery. Ultra Slim-Fast or Carnation Instant Breakfast prepared with nonfat milk or Lactaid, or MET-Rx mixed with water, were used to provide 45–60 g of protein daily. Allowable fluids were water, sugar-free Popsicles (less than 25 calories each), tomato or V8 juice, Crystal Light or other sugar-free, noncarbohydrate beverage, sugar-free cocoa, decaconated (“flat”) diet soda or seltzer water, bouillon or broth, diluted unsweetened fruit juices, and diet j ell-O. Six weeks after surgery the stage IV diet consisting of soft or pureed high-protein food was begun. The stage III liquids were allowed, as was fish (avoiding salmon, catfish, and trout), pureed water-packed tuna, pureed shellfish, skinless boiled and pureed chicken or turkey breast, and nonfat cottage cheese. Two months after surgery the final stage V diet was allowed. Regular solid foods were eaten in small volumes and tailored for 45–60 g of daily protein ingestion. All foods that the patient could tolerate were allowed except nuts, seeds, chips, cheese, pizza, salad dressing, mayonnaise, red meat (including pork), lamb and veal, ice cream, frozen yogurt, and nonfat yogurt.

Follow-up. Patients were seen 2 weeks after surgery for wound check and dietary counseling. They were followed monthly for the first 3 months following surgery and then at 6-month intervals.

Modeling weight loss. The differential equations we used to describe weight loss were

$$\frac{dW_t}{dt} = -k_1 W_t,$$  
(1)

The solution of this equation yields

$$W_t(t) = W_0 e^{-kt},$$  
(2)

where $W_0$ is the total body weight in kilograms at time $t$, $W_t$ is the initial total body weight, and $k_1$ is the exponential decay constant associated with total body weight loss. Differing weight loss rates between the fat and lean body compartments were modeled as a biexponential phenomenon. The model was developed from the following differential equation:

$$\frac{dW_t}{dt} = -k_1 W_t + \left[-k_2 W_t \frac{dW_t}{dt}\right].$$  
(3)
The total weight loss will be the sum of the weight lost in the fat (\(W_f\)) and the lean (\(W_l\)) body compartments. Weight lost in the fat compartment should follow simple decay kinetics. However, the weight loss in the lean body compartment results from two different processes. Protein is lost in the muscle mass secondary to reduced caloric intake and is represented by the \(-k\times W\) term. A certain amount of the muscle mass is required to support the patient’s weight. With weight loss some muscle will be lost because of the reduced need to support the excess fat weight. Thus, muscle will be lost in proportion to the lost fat mass \(dW_f/\text{dt}\). Muscle loss secondary to reduced fat weight would be delayed in time relative to the fat loss, making the exact nature of the rate constants describing this relationship complex. We blended all these effects into the single constant \(k_t\). An approximate solution to Eq. (3) is

\[
W_f = \frac{k_f}{(k_f - k_l)} (W_f e^{-k_f t} + W_l e^{-k_l t}),
\]

where \(W_f\) and \(W_l\) are the initial fat and lean body masses determined by BIA. Weight loss and time data were fitted by nonlinear regression using the NCSS statistical package (NCSS, Kaysville, UT). Determination of whether the biexponential equation provided a significantly improved fit relative to the monoexponential equation was made by the \(F\) test [23].

Prospective validation of the equation. Following development of the equation coefficients, a group of 30 consecutive patients was followed with serial body weight measurements after gastric bypass surgery. Each had BIA measurements obtained preoperatively and then was weighed at various intervals after surgery for as long as 6 months. The calculated weights at each time interval were compared to the measured weights by linear regression.

Statistical analysis. Calculations of mean and SEM were made using Microsoft Excel Version 97 (Microsoft Corporation, Redmond, WA). Percentage excess weight loss was calculated by using the formula \(100 \times (\text{initial weight} - \text{final weight})/(\text{initial weight} - \text{target weight})\). Group comparisons were performed with \(t\) tests (NCSS).

RESULTS

Twenty-four females and four males were included in this study. The mean age for these patients was 42 ± 2 years (range, 21–57 years). Their initial weight was 145.4 ± 4.6 kg (320 ± 10 lb), and the BMI was 51.3 ± 2 kg/m². Based on BIA determinations the mean preoperative lean body mass was 71.4 ± 2.2 kg (157 ± 5 lb), with the fat mass being 74.2 ± 3.3 kg (163 ± 7 lb). The fat mass ranged from 55.8 to 103.0 kg (123–227 lb).

Repeat BIA determinations were made 11 ± 1 months (range, 4–24 months) after the surgery. At that time the average weight was 99.4 ± 4.3 kg (218 ± 10 lb). The final measured BMI was 35.0 ± 1.6 kg/m². The mean weight loss was 46.0 ± 3.0 kg (101 ± 7 lb). The final lean mass was 58.7 ± 2.3 kg (129 ± 5 lb), with the weight being 41.6 ± 3.1 kg (92 ± 7 lb), corresponding to 39.7 ± 1.5% body fat. Using the Metropolitan Life Insurance tables to define target weights, patients lost 59 ± 3.2% of excess weight.

Of the weight lost, 73% was from fat loss and 27% from lean body mass loss. The average basal metabolic rate decreased from 2171 ± 62 kcal before surgery to 1795 ± 65 kcal after surgery. Loss of fat mass as measured by serial BIA measurements is presented in Fig. 1. Fat loss is represented as a percentage of the initial fat weight on the ordinate, and the time in months is on the plot’s axis. The curve decays monoexponentially. Nonlinear regression revealed a decay constant of 5.42 ± 0.36 × 10⁻² per month. The ratio of the residual to total sum of the squares for the fit was 96.7%. Figure 2 demonstrates the rate of lean body mass lost versus time. Lean body mass decreases less slowly than fat, and nonlinear regression yielded a decay constant of 1.54 ± 0.22 × 10⁻² per month. The ratio of residual to total sum of the squares was 98.3%. The relationship between lean and fat body weight is demonstrated in Fig. 3. Plotting the lean weight as measured by BIA on the ordinate and fat weight on the axis demonstrated an almost linear relationship between them. With larger fat weights there is a commensurate increase in lean body mass, suggesting that lean mass increases to support the extra weight of accumulated fat. Linear regression resulted in the following equation: lean weight = 0.37 × fat weight + 41.4 (\(r = 0.82\)), where the weights are in kilograms.

During the secondary follow-up period, 16 of the original 28 patients could be located. The median follow-up time was 33 ± 2 months (range, 22–50 months). The mean final weight was 94.0 ± 5.7 kg (207 ± 13 lb), which was not significantly different from the weight observed at the initial follow-up period. Figure 4 demonstrates the weight loss pattern in this population of patients. Comorbid conditions were...
assessed for their response to weight loss. To be accepted for surgery in our program, patients must have a body mass index greater than 40 and a weight-related comorbidity. All patients in this series had at least one of the following: hypertension, osteoarthritis, sleep apnea, or diabetes. We also assessed the effect of weight loss on depression, asthma, and gastroesophageal reflux. Table 1 demonstrates that weight loss resulting from RYGB improved or cured all these conditions, with two exceptions. One patient had worse reflux symptoms following RYGB and another had no improvement in orthopedic pain after the weight loss. Hypertension was cured in three patients. Diabetes resolved following gastric bypass in three patients. Six had complete resolution of orthopedic pain and five were cured of sleep apnea.

Modeling of the weight loss data to a monoexponential decay function by nonlinear regression with Eq. (2),

\[ W_T(t) = W_{T0} e^{-k_T t}, \]

resulted in \( k_T = 1.88 \pm 0.20 \times 10^{-2} \) per month, with the ratio of residual to total sum of the squares 94.3%. Fitting the biexponential equation,

\[ W_T = \frac{k_f}{(k_f - k_i)} (W_{T0} e^{-k_T t} + W_{i0} e^{-k_i t}), \]
resulted in $k_f = 7.61 \pm 1.27 \times 10^{-2}$ per month and $k_t = -0.93 \pm 0.13 \times 10^{-2}$ per month, with the ratio of residual sum of the squares to the total sum of the squares 98.8%. F test revealed that the biexponential equation provided a significantly better fit than did the monoexponential formula, irrespective of the fact that the biexponential model has more parameters to fit ($P < 0.001$). Figure 5 plots the estimated final weight by the monoexponential formula against the measured final weight. The solid line represents the identity line where the estimated value equals the measured one. Figure 6 is similar except that it plots the weight estimated with the biexponential model. The graphs confirm the improved predictive power of the biexponential model.

Prospective analysis of the equation's ability to predict weight loss was determined from a series of 130 measurements made in 30 consecutive patients during a 6-month time interval following gastric bypass. Linear regression of the observed versus predicted weight loss confirmed the equation's validity. The regression equation was the following: observed weight $= 0.89 \times$ predicted weight $+ 7.73$, $r = 0.89$, $P < 0.0001$. The regression slope was close to the identity line of 1.0 and was statistically significant, suggesting that the equation accurately predicted weight loss.

Figure 7 plots the last measured weight against the patients' initial weight. The axis is ordered from the heaviest to the lightest patient. The triangles represent the ideal weight for a particular patient derived from the Metropolitan Height/Weight table. Squares represent the estimated weight from the biexponential equation. The measured and predicted weight graphs nearly overlay each other. Figure 8 demonstrates the effect of initial body composition on the expected weight loss curve for a 150-kg patient. The top curve represents a patient with 40% fat initially, the middle, 50%, and the bottom, 60%. The rate and final amount of weight loss differs for each of these three scenarios.

**DISCUSSION**

We developed a mathematical model using BIA measurements that accurately predicted weight loss rate and magnitude following gastric bypass surgery. Treating the body as one compartment and modeling...
weight loss with a monoexponential model produced erroneous estimates of the final weight. Our study showed why this model failed and culminated in the derivation of a more physiologic biexponential weight loss model.

Human obesity results from increases in both fat and lean body mass. The increased lean mass results from the need to carry excess weight from fat. Body composition studies have demonstrated that for a given height, increased weight is accounted for by excess tissue composed of 75% percent fat and 25% lean mass [24, 25]. Using BIA, we found that RYGB surgery resulted in loss of 27% lean body tissue and 73% fat tissue and that these losses followed monoexponential decay kinetics (Figs. 1 and 2). Thus, compositional weight loss following gastric bypass is proportionate to the excesses that exist in the fat and lean body compartments. Similar, proportional weight loss was observed in response to medically induced weight loss [26]. In contrast, operations reliant on malabsorption result in excessive loss of lean body mass [27].

The fat compartment lost weight much more rapidly than did the lean compartment. Because the compartments lose weight at different rates and to differing extents, the total amount of weight loss will be dependent upon the initial amounts of weight in each compartment. The effect of different initial body compositions is illustrated in Fig. 8. The top curve represents the anticipated weight loss for a 150-kg patient with 40% fat and 60% lean mass. The rate and final expected weight is much less than for an equivalent 150-kg patient with 60% fat and 40% lean body mass.
represented on the bottom curve. Because of the differential effect of compartmental weight loss, it is important to account for a patient’s initial body composition when attempting to predict their final weight with a weight loss program. The biexponential formula proposed in this work accounts for these differences and provides an accurate estimate for weight loss.

Nonlinear regression of serial BIA measurements revealed that compartmental weight loss follows monoeXponential kinetics. Under these circumstances one anticipates that the exponential decay constant will be negative, representing a downward-falling curve. When the biexponential model was fitted, the fat compartment decay constant was negative but the lean compartment’s was positive. In deriving the differential equation for the lean compartment we aggregated several phenomena into its decay constant. Weight loss in the fat compartment falls because patients enter negative energy balance following weight loss surgery. The calorie deficit results in loss of the fat mass that should have exponential decay kinetics. Loss of lean body mass is more complex and results from two distinct phenomena. Postsurgical caloric deficits result in lost muscle mass from protein wasting. Muscle is necessary to support the body’s weight. Following loss of fat mass, less muscle is required to support the total body weight. We found that the total amount of muscle mass was linearly correlated with the total amount of fat mass (Fig. 3). Numerous studies have demonstrated that lean body mass increases proportionately to increased fat mass [24, 25] and that they both decrease in the same proportions with weight loss [26]. The muscle mass will be lost proportionately to the lost fat mass and will temporally lag behind the loss of fat weight. We modeled this effect in the biexponential equation by including the term dW/dt in the lean body compartment term (see Methods for a more detailed explanation of the rationale for the differential equations). The constant k, accounts for the exponential loss of lean body mass secondary to caloric deficits and the time-delayed change in fat weight. In deriving a total body weight loss–predicting equation it was not important to model each of these effects; rather, they were all aggregated into the single constant k,. Thus, the decay constant in the biexponential model for lean body mass does not resemble the one for the monoeXponential decay of muscle mass as measured by a BIA. However, the decay constant k, = 7.61 ± 1.27 × 10⁻² per month, predicted with the biexponential equation, was similar to that estimated from the BIA measurements for fat weight loss, 5.42 ± 0.36 × 10⁻² per month.

Because the bioelectrical properties for obese people may differ from those of their lean counterparts, application of BIA measurements in obese patients has not been universally accepted. Electrolytes dissolved in the various water-containing compartments conduct electricity, and the overall conductance is proportional to the total body water content. Resistance to an alternating current, i.e., the impedance, is inversely proportional to the conductance. Muscle is highly conductive because the intracellular compartment has a high electrolyte concentration. Although the muscular compartment is the principle conductor of electrical current, fat, blood, and bone also conduct electricity. Fat has a low intracellular content of dissolved electrolytes and resists current passage. Each compartment contributes to the total body electrical impedance proportionately to its mass and electrical properties. From the total body weight the relative amount of body fat and muscle can be determined from BIA measurements [21]. Because of the complexity of the various interactions, BIA measurements cannot be related to the lean body mass by any simple mathematical formula. BIA devices used clinically are calibrated by comparing impedance measurements to lean body mass measured by other techniques [18, 22, 28].

Obesity is associated with an increase in extracellular water [29] that by its nature is conductive and, therefore, lowers impedance. For this reason BIA estimates of lean and fat body mass in obesity may be inaccurate for a unit calibrated on nonobese individuals. The device used in our study has been calibrated for obesity and utilizes four different equations for males and three for females [22]. The equations are selected internally by the machine by using sex, height, and weight criteria to maximize the precision of lean body mass estimates from BIA measurements.

Obesity results in hyperlipidemia, hypertension, diabetes, sleep apnea, and osteoarthritis. Osteoarthritis limits patients’ mobility and restricts their ability to exercise, resulting in continued weight gain. Sleep apnea interrupts normal sleep such that obese patients are constantly tired or in severe cases fall asleep during the day. This is particularly hazardous when it occurs while driving. Hyperlipidemia, hypertension, and diabetes accelerate the development of atherosclerotic cardiovascular disease. Ultimately, obese patients have significantly reduced longevity and the primary cause for early mortality is the high incidence of cardiovascular disease [30–32]. Relatively modest amounts of weight loss on the order of 10% substantially reduce the severity of obesity-related comorbid conditions, culminating improved longevity [33]. Although small amounts of weight loss improve outcomes, what the final or target weight should be remains unknown. Many studies have used published weight-for-height tables for target weight determination. When these are used, gastric bypass results in approximately 60% excess weight loss. Although frequently used for establishing a target for weight loss programs, the tables have little relevance for obese patients. The Metropolitan Life weight-for-height table
is the most frequently used for determination of the ideal body weight. For any given height, the table provides the weight that was associated with the greatest life span for young, healthy individuals who purchased life insurance [14]. No study has shown that obese patients achieving these weights will have greater longevity, nor has any study demonstrated what the ideal weight should be after an obese patient loses weight. Since obesity surgery is known to control the comorbid conditions that reduce life span and because modest degrees of weight loss are associated with increased longevity [34, 35], the primary goal for weight loss surgery should be reduction in life-limiting comorbid conditions. Achieving an arbitrarily set target weight should be a secondary and, therefore, less important goal. This is important because various operations have been proposed that result in greater weight loss than the gastric bypass in order to more closely approximate the ideal body weight found in the Metropolitan Life table. All of the operations potentially have more complications than the gastric bypass. Because the additional weight loss they induce will not necessarily benefit patients, these operations should be studied by randomized controlled trials with long-term follow-up to determine if they are truly superior to the gastric bypass. The weight loss–predicting equation we have developed in this study provides the weight a patient can reasonably be expected to achieve following gastric bypass surgery. Knowing this weight facilitates appropriate counseling for patients regarding the expected weight loss outcome from gastric bypass procedures.

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