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ORIGINAL CONTRIBUTIONS

Patterns of Weight Loss Response Following Gastric Bypass and Sleeve Gastrectomy

Ana de Hollanda · Tania Ruiz · Amanda Jiménez · Lílliam Flores · Antonio Lacy · Josep Vidal

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Abstract

Background Despite the health benefits of bariatric surgery (BS) extend beyond WL, better understanding of the WL response may help improve the outcomes of BS. In this context, we aimed to assess patterns within the variability of weight loss (WL) after Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG).

Methods WL data from 658 subjects that underwent RYGB (n=464) or SG (n=194) as first BS were analyzed. Based on excess WL (EWL), subjects were categorized as good WL responders (EWL≥50 % at nadir weight and throughout follow-up), primarily poor WL responders (1-PWL:EWL<50 % at nadir weight and thereafter), and secondarily poor WL responders (2-PWL:EWL≥50 % at nadir weight, but <50 % at last follow-up visit). Predictors associated with different WL outcomes were ascertained using regression analysis.

Results Median follow-up was 55.7 months. Nadir EWL ranged 12.4–143.6 %; last follow-up visit EWL ranged −22.1–143.6 % and weight regain (WR) ranged 0–64.1 kg. Good WL was found in 75.7 of the cohort. 1-PWL response (4.7 %) was characterized by lesser WL but similar WR as compared to good WL and was associated with larger BMI and diabetes prior to surgery. 2-PWL response (19.6 %) was characterized by larger WR as compared to the other groups and was more common following SG. Lesser percentage of medical appointments kept was associated with 1-PWL and 2-PWL.

Conclusion Our data show the high inter-individual variability of the WL response at mid-term after RYGB and SG and that poor WL after BS could be illustrated by two different patterns, characterized either by sustained limited WL (1-PWL), or pronounced weight regain (2-PWL).

Keywords Gastric bypass · Sleeve gastrectomy · Weight loss

A. de Hollanda · A. Jiménez · L. Flores · A. Lacy · J. Vidal (✉)
Obesity Unit, Endocrinology and Nutrition Department, Hospital Clinic Universitari, Villarroel 170, 08036 Barcelona, Spain
e-mail: jovidal@clinic.ub.es

T. Ruiz
Department of Nutrition and Food Sciences, University of Barcelona, Barcelona, Spain

A. Jiménez · L. Flores · J. Vidal
Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Barcelona, Spain

A. Jiménez · L. Flores · A. Lacy · J. Vidal
Institut d'Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Barcelona, Spain

Introduction

It is well established that the health benefits of bariatric surgery (BS) extend beyond weight loss (WL) [1, 2]. Nonetheless, several lines of evidence suggest that WL is an important contributor to the health outcomes associated with BS [3, 4]. Thus, it is conceivable that better understanding of the WL response to BS techniques may help delineate strategies to optimize this therapeutic approach.

Undoubtedly, BS is the best available therapy to achieve and sustain significant WL in morbidly obese subjects [2]. However, several studies have shown that postsurgical WL varies widely and a sizable proportion of subjects present a relatively poor response [2, 5–8]. In the landmark Swedish Obese Subjects (SOS) study, maximum WL after surgery averaged approximately 34 kg but ranged between −95.5 and +2.0 kg [5]. Furthermore, in that study, nadir weight was ensued by gradual weight regain averaging 11.8 kg but ranging between 0.0 and 51.4 kg by 6 years after surgery. Similarly, the 95 % confidence interval for excess WL (EWL) ranged between 70.1 and 84.9 % at 3 years and between 42.7

and 63.9 % at 6 years in a small cohort of subjects that underwent sleeve gastrectomy (SG), another commonly performed BS technique [7]. The above mentioned studies nicely describe the substantial variability in weight change following BS. Nonetheless, description of patterns of weight change within this variability has seldom been attempted [2]. It could be hypothesized that characterization of different weight loss patterns may help advance the identification of factors associated with variable weight loss following BS.

Against this background, the primary aim of our study was to describe the presence of different patterns of WL up to 5 years of follow-up after two commonly performed BS techniques, namely Roux-en-Y gastric bypass (RYGB) and SG. As secondary aim, we examined pre-surgical predictors of such postsurgical WL outcomes.

Subjects and Methods

Participants in our retrospective analysis of prospectively collected data were selected among the 945 subjects that underwent BS surgery at our institution between 2005 and 2009. Eligibility criteria included age ≥18 years, first-time RYGB or SG surgery, and ≥30 months of available follow-up. Patients were considered for BS based on the current guidelines [9]. The technical aspects and the criteria for selection of RYGB or SG at our institution have previously been reported [10, 11]. In brief, laparoscopic RYGB included the creation of a small proximal gastric pouch of about 20 mL along the lesser curvature of the stomach, the division of the jejunum 40 cm distal to the ligament of Treitz, an end-to-side gastrojejunostomy of about 1.5 cm in diameter using a circular stapler, and a side-to-side jejunojejunostomy 150 cm distal to the gastrojejunostomy. For the SG, the greater curvature including the complete fundus was resected from the distal antrum (5 cm proximal to the pylorus) to the angle of His. A laparoscopic stapler, EndoGIA (Autosuture, Norwalk, CT, USA) with a 60-mm cartridge (3.5-mm staple height, blue load), was used to divide the stomach alongside a 34 French bougie (placed against the lesser curvature of the stomach). Following approval by the local ethics committee, written informed consent was obtained from all study participants.

Data was prospectively collected prior to surgery and at 4, 8, 12, 18, 24, 30, 36, 48, and 60 months in the postsurgical period. A diagnosis of type 2 diabetes mellitus (T2DM), hypertension, dyslipidemia, sleep apnea syndrome, and tobacco use was based on medical history and laboratory data. Body weight, height, and waist circumference were measured as previously described [10]. Postoperative WL was expressed as a percentage of the pre-surgical excess weight (% EWL=[100×(weight prior to surgery−weight at the time of evaluation)/(weight prior to surgery−weight corresponding to body mass index (BMI)=25 kg/m^2)]). Maximum WL was described as the maximum EWL recorded at postsurgical checkup visits. Weight regain was defined as the difference between body weight at last follow-up and nadir weight and was expressed in kilograms or as percent of maximum WL. Medical appointments kept were calculated as the percent of visits attended out of the nine scheduled postsurgical medical visits.

Three different patterns of WL were pre-specified based on the EWL Reinhold criteria modified by Christou et al. [8]. Patients with EWL>50 % at nadir and throughout subsequent follow-up were considered as good WL responders. Patients with EWL<50 % at nadir weight and up to the end of follow-up were considered as primarily poor WL (1-PWL) responders. Subjects with EWL≥50 % at nadir weight but EWL<50 % at last follow-up at visit were considered as secondarily poor WL (2-PWL) responders. Time to adjudication of a 2-PWL response was defined as the time elapsed between surgery and the study visit at which EWL<50 % was first recorded following nadir weight. Patients that underwent SG as primary BS procedure but went through revisional BS were classified as 1-PWL responders or 2-PWL responders based on the WL trajectory up to the time of the second surgery.

All data are expressed as mean±SD unless stated otherwise. Differences between groups were evaluated using parametric or non-parametric test as appropriate. Predictive factors of the different WL outcomes were ascertained by logistic regression analysis. Clinical features associated with 2-PWL response were evaluated by means of logistic and Cox regression analysis, the latter to take into account the time of follow-up. Survival analysis was used to compare occurrence of a 2-PWL response over time following RYGB and SG. Statistical analyses were performed using the SPSS 20.0 statistical package, and significance was set at a p value of <0.05.

Results

Table 1 displays the clinical characteristics of the study of 658 participants. Out of the original 945 potentially eligible patients, 50 (5.0 %) were excluded as current BS that was not a primary procedure, 23 (2.4 %) as revisional surgery for SG was performed <30 months (mainly because of severe gastroesophageal reflux), and 237 (25.0 %) because lack of follow-up beyond 30 months. At the time of surgery, age ranged from 18 to 69 years and BMI from 35 to 84 kg/m^2. RYGB and SG were performed, respectively, in 70.5 and 29.5 % of the cohort. Because of our criteria for the selection of the surgical technique, subjects that underwent SG presented larger BMI, waist circumference, and more commonly a diagnosis of T2DM, hypertension, and dyslipidemia. Moreover, male gender ($p<0.001$) and older age ($p<0.01$) were found in SG subjects.

Table 1 Clinical characteristics of the study participants at baseline

	Whole cohort	Gastric bypass	Sleeve gastrectomy
n	658	464	194
Gender (% female)	74.5	78.4	64.9[c]
Age (years)	45.3±11.0	44.6±10.1	47.1±12.4[b]
BMI (kg/m^2)	47.1±6.5	45.6±5.0	50.7±8.2[c]
Waist circumference (cm)	132±15	128±13	140±17[c]
Diabetes mellitus (%)	27.8	25.6	33.0 (p=0.057)
Hypertension (%)	41.5	37.2	51.5[a]
Dyslipidemia (%)	25.5	23.0	31.4
Tobacco use (%)	22.2	22.6	21.1
Sleep apnea syndrome (%)	18.1	16.8	21.1

Data are expressed as mean±SD

BMI body mass index

[a] $p<0.05$; [b] $p<0.01$; [c] $p<0.001$ (for the comparison between gastric bypass and sleeve gastrectomy groups)

In the entire cohort, median postoperative follow-up was 55.7 months (range 30–68 months). Weight loss was maximal (nadir weight) at 23.7±15.7 months after surgery, and at that time, EWL was 81.7±19.2 %. At last evaluation, EWL was 65.3±22.8 % (corresponding to a weight regain of 9.2±8.4 kg or 20.9±11.9 % relative to nadir weight). The three WL parameters showed high inter-individual variability with maximum EWL ranging 12.4 to 143.6 %, EWL at last checkup −22.1 to 143.6 %, and weight regain 0 to 64.1 kg. Length of follow-up was larger in RYGB as compared to SG subjects (respectively 54.3±9.2 and 48.8±10.8 months; $p<0.001$). Analysis of covariance with gender, age, BMI, prevalence of T2DM, hypertension, and length of follow-up as covariates showed EWL at nadir (adjusted marginal mean±standard error; RYGB 81.3±0.8 versus SG 83.0±1.4 %) and time to nadir weight (RYGB 24.4±0.7 versus SG 22.2±1.2 months) were not significantly different between surgical cohorts (respectively $p=0.952$ and $p=0.136$). Weight regain was smaller after RYGB (RYGB 8.6±0.4 kg or 19.5±0.9 % versus SG 10.6±0.6 kg or 24.1±1.4 %; both $p<0.01$).

At last follow-up visit, 498 (75.7 %) of the study participants presented EWL≥50 % and were thus considered as good WL responders. In contrast, EWL<50 % was encountered in 160 (24.3 %) subjects, with 31 (4.7 %) and 129 (19.6 %) being classified, respectively, as 1-PWL responders or 2-PWL responders according to the pre-specified criteria. The EWL trajectories of these three groups of subjects are presented in Fig. 1. Of note, the EWL=50 % at maximum WL corresponded to the 5th percentile of the EWL distribution of the whole cohort at nadir weight. The EWL=50 % corresponded to the 12th, 15th, 23rd, or 27th percentile of the WL distribution, respectively, at 30, 36, 48, or 60 months follow-up. As shown in Table 2, differences in EWL between the good WL responders group and the 2-PWL responder group were already apparent at maximum WL ($p<0.001$). Weight regain in the good WL responders group ranged between 0 and 64.1 kg and was significantly less as compared to the 2-PWL responder group (range 4.3 to 57.6; $p<0.001$) (Table 2). Weight regain in the 1-PWL responder group ranged from 0 to 25.8 kg ($p=0.265$ and <0.001, respectively, compared to good WL and 2-PWL responder groups) (Table 2).

Comparison (ANOVA analysis) of the clinical characteristics of study subjects based on WL outcomes is shown in Table 2. Logistic regression analysis showed that 1-PWL response was independently associated with higher BMI [OR 1.060 (95 % confidence interval, CI, 1.060–1.060), $p=0.024$], pre-surgical diagnosis of T2DM [OR 2.407 (95 % CI 1.047–5.532), $p=0.039$], and the percentage of postsurgical medical appointments kept [OR 0.963 (95 % CI 0.943–0.983), $p<0.001$]. Since weight regain over time characterized 2-PWL response, Cox regression analysis was performed to evaluate the independent contribution of clinical variables to this WL pattern. The analysis demonstrated that SG [OR 1.775 (95 % CI 1.167–2.700), $p<0.01$], albeit marginally, a lower BMI [OR 0.970 (95 % CI 0.943–0.998), $p=0.035$], and the percentage of postsurgical medical appointments kept [OR 0.953 (95 % CI 0.940–0.966), $p<0.001$] were significant predictors of 2-PWL response. Survival analysis with Kaplan-Meier as estimate showed that adjudication of a 2-PWL response occurred not only more often but also earlier in subjects that underwent SG (time to EWL<50 % of subjects in the secondary WL failure group: SG, 44.6±2.2 versus RYGB, 52.7±2.1 months; $p=0.01$).

Discussion

Our data obtained at a median of 4.5 years after surgery illustrate the high inter-individual variability in the WL response to RYGB and SG, two commonly and currently performed BS techniques, that could be depicted in three distinct patterns of WL. First, a good WL response pattern characterized by EWL>50 % both at maximum WL and last follow-up visit, occurring in three out of four of the study participants.

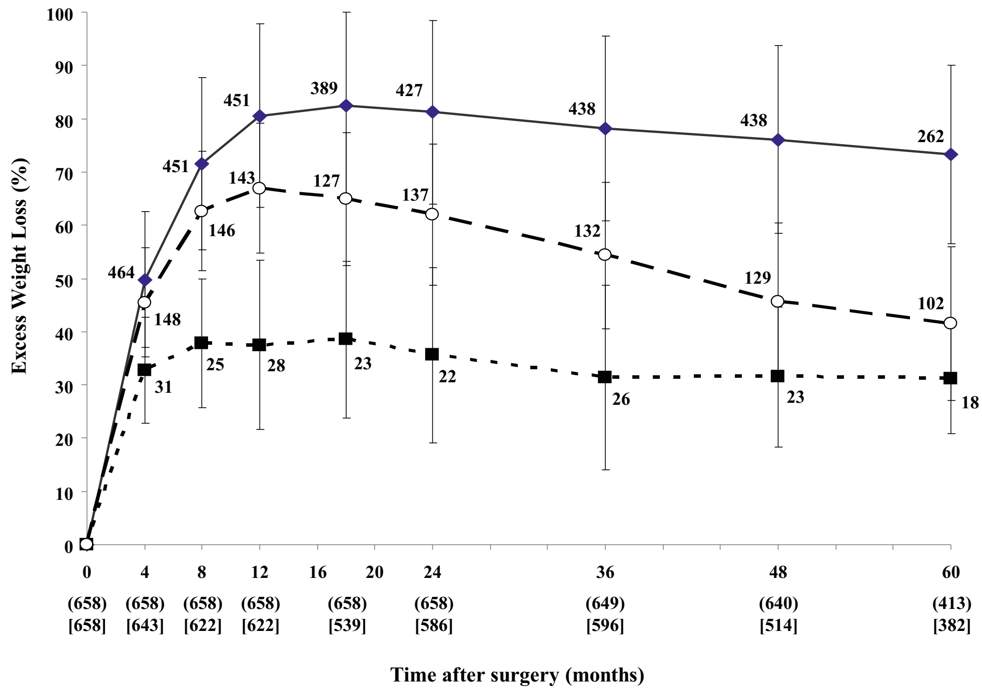

Fig. 1 Excess weight loss over 5 years in subjects with good weight loss (WL) response, primarily poor WL response, and secondarily poor WL failure. *Blue diamonds*, *solid line*: good WL group; *open circles*, *dashed line*: secondarily poor WL responders group; *black squares*, *dashed line*: primarily poor WL responders group. The number of patients in each category that contributed to each time point is shown next to each point on the graph. The number of patients that were eligible for follow-up and the number of patients evaluated at each time point are shown, respectively, *between parentheses* and *squared brackets* below the *X*-axis

Second, a less common 1-PWL response pattern was characterized by poor WL and no major weight regain, resulting in EWL<50 % throughout follow-up. Third, a 2-PWL response pattern was characterized by limited but larger than 50 % EWL at nadir and progressive subsequent weight regain, occurring in about 1 out of 5 study subjects.

Table 2 Clinical characteristics at baseline and weight loss (WL) parameters of study subjects according to the three different WL patterns

	Good WL response	Primarily poor WL response	Secondarily poor WL response	*p* value
n	498	31	129	
Gender (% female)	76.1	70.9	69.0	0.330
Age (years)	44.7±11.0	47.5±10.5	47.2±10.6	0.037
BMI (kg/m^2)	47.0±6.8	49.7±6.1	46.9±5.6	0.068
Waist circumference (cm)	132±15	137±15	132±13	0.118
Type of surgery (% GBP)	72.6	61.2	70.6	0.323
Diabetes mellitus (%)	24.7[a, 1]	45.1	35.7	0.005
Hypertension (%)	38.4[a, 1]	51.6	50.4	0.022
Dyslipidemia (%)	24.6	25.8	27.4	0.857
Tobacco use (%)	24.5	12.9	15.5	0.034
Sleep apnea syndrome (%)	15.5 [a, 1]	16.1	28.7	0.013
Maximum EWL (%)	87.7±16.3[b, 2]	43.4±13.1[#]	68.5±11.5	<0.001
Time to maximum EWL (months)	24.5±13.2[a,1]	17.3±11.8	15.3±7.2	<0.001
EWL at last follow-up visit (%)	74.6±16.9[b, 2]	31.7±14.2	38.4±12.9	<0.001
Weight regain (Kg from BW at nadir)	7.3±7.[b, 2]	7.9±7.1[#]	16.7±9.3	<0.001
Postsurgical medical appointments kept (%)	87.3±15.4[a]	77.4±23.3[#]	88.9±13.5	<0.001

Data are expressed as mean±SD. *p* value for the comparison among the three WL groups

BMI body mass index, *EWL* excess weight loss, *BW* body weight

[a] $p<0.05$; [b] $p<0.001$ (for the post hoc comparison between the good WL response and primarily poor WL response groups); [1] $p<0.001$; [2] $p<0.01$ (for the post hoc comparison between the good WL response and secondarily poor WL response groups); [#] $p<0.001$ (for the post hoc comparison between the primarily poor WL response and secondarily poor WL response groups)

The high inter-individual variability in the long-term WL response following BS found in our study confirms previous data following RYGB and expands this finding to the increasingly performed SG. The overall WL response to RYGB found in our study is similar to that previously reported in studies including data beyond 5 years of follow-up [5, 6, 8, 12–14]. Unfortunately, although increasingly performed, long-term data following SG is limited. A recent systematic review of randomized clinical trials including a SG-arm showed %EWL that ranged from 49 to 81 % at 6 months to 3 years follow-up [15]. Similarly, systematic review of SG series with longer follow-up showed %EWL that averaged between 43 and 86 % [16]. However, the number of patients was small ($n \leq 60$) in all the contributing studies to that of systematic review. Of note, Prevot et al. recently reported variable EWL (43±25 %) at 5 years follow-up in a series of SG only patients ($n=84$), with 42 % of them presenting EWL <50 % at last follow-up visit [17]. Our findings of no difference in maximum WL but larger weight regain following SG as compared to RYGB are in agreement with the 3-year follow-up data from a recently reported RCT in subjects with T2DM comparing these two surgical techniques with medical therapy [18].

As mentioned above, our data suggest that variable WL response following RYGB and SG could be depicted in three different patterns: good WL response, 1-PWL response, and 2-PWL response. We acknowledge the EWL criteria chosen to define these trajectories were arbitrary though based in current literature and have recently been challenged [19]. As expected from its static nature, the EWL<50 % criteria corresponded to different percent values when applied to the distributions of maximum or last follow-up visit WL. Nonetheless, we used this criterion because of lack of consensus on how insufficient WL following BS should be defined. Considering the limitations above that the WL response in our poor WL groups was limited is demonstrated by their positioning in the poorest quartile of the WL distribution in our cohort. Interestingly, although 1-PWL responders presented by definition lower EWL at maximum WL, they presented with similar weight regain as compared to good WL responders. In contrast, 2-PWL responders were characterized by larger weight regain as compared to good WL and 1-PWL responders. Thus, we would suggest that our pre-specified definition of the two poor WL trajectories was clinically meaningful as it discriminated between subjects that did no achieve adequate postsurgical WL throughout follow-up from those in whom the long-term outcome was determined mainly by marked weight regain. Interestingly, using mathematical modeling up to five distinct WL trajectories have recently been reported in subjects that had undergone RYGB [2]. Although different criteria to those reported herein were used, approximately 24 % of the subjects included in the study presented with a WL<25 % relative to baseline. Interestingly, 2 % of the whole cohort presented no further WL after 6 months of follow-up and WL of approximately 10 % after 3 years.

Reviews on the large body of available research on clinical predictors of WL response as continuous variable following BS have previously been reported [20–22]. Studies in the literature differ in how WL was assessed, the clinical predictors tested, and the length of follow-up used for the assessment. Although our study aimed primarily at providing a framework for future assessments of factors associated with postsurgical WL as trajectories, analysis of a limited set of factors in our series yielded consistent results with previous literature in the field [20–23]. Higher pre-surgical BMI, presurgical T2DM, and lower number of postsurgical appointments kept have been identified as associated to lesser EWL (assessed as continuous variable) after BS. Importantly, Cox regression analysis in our cohort showed that SG was associated with increased odds of 2-PWL response as compared to RYGB. Of note, this effect was not apparent when data was analyzed only up to 4 years follow-up (data not shown). Thus, our data underscore the importance of long-term follow-up when comparing the WL results of these two commonly performed BS techniques. Interestingly, except for the number of appointments kept, the set of factors associated with 1-PWL or 2-PWL in our series was distinct. In this context, we consider that our data may provide a framework that may help advance in the identification of factors associated with variable WL after BS. We would hypothesize factors associated with resistance to WL would potentially underlie the 1-PWL response. In contrast, factors facilitating weight regain would largely lie beneath 2-PWL response. We acknowledge that, unfortunately, we evaluated a very limited set of clinical factors precluding definite testing of these hypotheses. Thus, future studies are warranted to evaluate the association of these phenotypes with a comprehensive set of clinical [20–23], genetic [5, 24], or hormonal factors [22] potentially involved in the variable postsurgical response.

We acknowledge that our study has several limitations. As mentioned above, while we used criteria based on the literature, these criteria could be viewed as arbitrary in defining the WL response ensuing BS [19]. In fact, several clinicians in the field of BS would argue that resolution of comorbidities and quality of life is of greater relevance to the outcomes of BS than a WL above certain threshold [20]. Undoubtedly, we acknowledge the many health benefits of BS beyond WL [1, 25]. We fully endorse that multiple rather than single outcomes need to be considered when evaluating the overall health impact of BS [20]. Nonetheless, herein, we rather focused in WL as single outcome as WL after BS because of the relevance of sustained weight reduction for the resolution of obesity-associated comorbidities [2, 3], and the potential health burden associated with persistent obesity resulting from poor WL response or weight regain after BS. Second, albeit the proportion of missing data in our series was comparable to that in previous studies in the field [13, 16, 17], we recognize this as limitation of our observational study. Importantly, at baseline, those lost to follow-up were not significantly different to those included in the study in the clinical characteristics that were independently associated with the different WL patterns. Third, we acknowledge that lack of randomization precludes definite conclusion of the comparisons between RYGB and SG. Finally, we acknowledge that we failed to provide a comprehensive analysis of the many factors potentially associated with the different WL phenotypes proposed in our analysis.

In summary, our analysis further illustrates the high inter-individual variability of the WL response at mid-term following BS. Within the limitations of lack of consensus definition, our data show that poor WL after RYGB and SG could be illustrated by two different patterns: (1) a primarily poor WL response pattern characterized by limited WL throughout follow-up encountered in approximately 5 % of subjects and at comparable rates following the two types of surgeries and (2) a secondarily poor WL pattern characterized by significant WL but subsequent weight regain leading to a final EWL<50 % encountered in approximately 20 % of subjects. Importantly, our data suggest that at a median follow-up of 4.5 years, the 2-PWL response is more commonly associated with SG as compared to RYGB. Our data on the occurrence of poor WL by no means should be interpreted as overall poor outcome of BS. Nonetheless, we propose further studies aiming at better understanding of the different WL trajectories after BS may foster maximization of the health benefits of this therapeutic approach.

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Authors' Contributions A. de H. and J.V. designed the study, analyzed the data, and wrote the manuscript. T.R. and A.J. analyzed the data and reviewed and edited the manuscript. A.L. and L.F. reviewed and edited the manuscript. J.V. is the guarantor of this work and as such, had full access to all the data in the studies, and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Conflict of Interest The authors have no conflict of interest to report relevant to this article.

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