Assessment of energy requirements in patients with short bowel syndrome by using the doubly labeled water method[1]

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ABSTRACT

Background: Short bowel syndrome (SBS) is a serious malabsorption disorder, and dietetic management of patients with SBS is extremely challenging. Once the degree of undernutrition has been assessed, successful dietary intervention is contingent on an accurate estimation and provision of energy needs.

Objective: We quantified total energy expenditure (TEE) in patients with SBS by using the doubly labeled water (DLW) method to inform energy needs and nutritional therapy goals.

Design: In this observational study, TEE was measured in 22 participants, 11 with SBS and 11 sex-, age-, and body mass index (BMI)–matched controls (non-SBS), for 14 d with the DLW method. Predicted energy requirements were determined by using the Escott-Stump equation and compared with TEE determined with DLW. Resting energy expenditure was measured by using indirect calorimetry, and an accelerometer was also used to determine physical activity level.

Results: Participants were aged (mean ± SD) 53 ± 8 y. Measured TEE was significantly higher than predicted TEE for the SBS group (1875 ± 276 compared with 1517 ± 175 kcal/d, $P = 0.001$) and also for the non-SBS group (2393 ± 445 compared with 1532 ± 178 kcal/d, $P < 0.01$). Measured TEE was significantly lower in the SBS group than in the non-SBS group ($P < 0.01$); however, predicted TEE did not differ significantly between the groups ($P = 0.84$). No significant differences were seen between measured and predicted resting energy expenditure either within or between groups.

Conclusions: Measured TEE in patients with SBS was significantly higher than predicted by using standard equations but also lower than values for age-, BMI-, and sex-matched non-SBS controls. Currently used formulas in clinical practice appear to underestimate energy requirements of patients with SBS, and revision is needed to prevent underfeeding and improve long-term prognosis. This trial was registered at clinicaltrials.gov as NCT02113228. *Am J Clin Nutr* 2016;103:77–82.

Keywords: short bowel syndrome, energy requirement, doubly labeled water, total energy expenditure, resting energy expenditure

INTRODUCTION

Short bowel syndrome (SBS)[4] is a complex disorder involving nutritional and metabolic changes that usually occur as a result of surgical resection of the jejunum and/or ilium (1, 2). The exact population prevalence of the syndrome is unknown and difficult to estimate for a variety of reasons, including variability in defining the syndrome and differing treatment and follow-up procedures. More recent data estimated that the annual prevalence of SBS in patients with nonmalignant bowel disease in the United States is 4 patients per 100,000 (3). Individuals with SBS typically have a reduced ability to absorb macronutrients such as fats, carbohydrates, and sugars, as well as vitamins, minerals, trace elements, and fluids (1).

The prognosis of patients with this diagnosis depends on the degree of resection and the magnitude of oral intake with frequent complications, including malnutrition, diarrhea, steatorrhea, specific nutrient deficiencies, and electrolyte imbalance (4). In addition to these specific problems, their compromised nutritional status can reduce quality of life and increase hospitalization, the rate of infections, and the risk of premature death (5). Thus, dietetic therapy providing adequate calories and nutrients is critical both for immediate prognosis and successful long-term rehabilitation.

There is currently little information on the actual energy requirements of patients with SBS. For intake to be "adequate," it is important to have an accurate estimation of energy requirements. In routine clinical practice, energy requirements in patients with SBS are calculated by using prediction formulas or estimates of calorie requirements per kilogram of body weight. However, it remains unknown if these equations (6) and calculations accurately estimate the energy needed to support optimal activities of daily living. It has been suggested that a substantial increase in energy intake may be required, particularly because adequate nutritional support has been clearly implicated as a factor in determining morbidity and mortality in these patients

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[4] Abbreviations used: DLW, doubly labeled water; IC, indirect calorimetry; PAL, physical activity level; REE, resting energy expenditure; SBS, short bowel syndrome; TEE, total energy expenditure; TPN, total parenteral nutrition.

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(7, 8). Inaccuracies in estimating caloric needs, using estimated energy requirements per kilogram of body weight or using prediction equations, may lead to negative energy balance that will negatively affect patient outcomes. Thus, studies to determine accurate energy requirements of patients with SBS are much needed to help direct diet management.

The aim of this study was to measure the total energy expenditure of patients with SBS and matched controls by using the doubly labeled water (DLW) method with a goal to better inform energy requirements and aid in the successful management of nutritional therapy in these patients.

METHODS

Subjects

We conducted a cross-sectional observational study in which a total of 22 participants, 11 with SBS (SBS group) and 11 matched participants without SBS (non-SBS group), were recruited. Free-living energy measurements were assessed for 14 d by using the DLW method (9). The baseline DLW assessment and days 7 and 14 were performed at the Metabolic Unit of the University Hospital at the Ribeirão Preto Medical School.

Participant recruitment and follow-up occurred between February 2013 and August 2014 by using a multistage process. Participants with SBS (SBS group) were recruited from the Metabolic Unit and the Ambulatory Nutrition Unit of the University Hospital at the Ribeirão Preto Medical School, São Paulo University. Adult patients, aged ≥18 y and diagnosed with SBS, were recruited to participate in the study. We excluded subjects with a history of cancer or those using medications that could affect energy metabolism.

Recruitment of matched controls—that is, participants without SBS (non-SBS group)—was completed by using extensive evaluation of electronic medical records and from the ambulatory units of the University Hospital, as well as via advertisements using the web (university intranet and Internet), radio, and television. Non-SBS patients were matched for characteristics similar to the patients with SBS by using a multistage filter: medical records were first filtered by using age and sex, and this yielded a larger data set with a mean of 24,000 records per patient with SBS. After this step, a weight filter was applied and yielded a shortlist with a mean of 106 records per patient with SBS. This list was then carefully reviewed for ethnicity, BMI, and chronic diseases to obtain the single best matched non-SBS control. It is to be noted that height was not systematically available in all records, and so a weight filter was first applied. Then, height was obtained for those records missing this information, and BMI (in kg/m^2) was calculated.

This study was approved by the Ethics Committee of Ribeirão Preto Medical School of São Paulo University (number 1822/2013) and conducted according to the Helsinki Declaration. All participants provided a written informed consent. This trial was registered at clinicaltrials.gov as NCT02113228.

Protocol

The protocol was implemented over a 14-d period. Participants were admitted to the Metabolic Unit of the University Hospital at the Ribeirão Preto Medical School, São Paulo University on days 0, 7, and 14. On day 0, the participants were fasted overnight for 12 h, and measurements including weight, height, bioelectrical impedance analysis, and resting energy expenditure (REE) were performed. Subjects also provided a baseline urine sample and were dosed with DLW to measure free-living energy expenditure. The activity monitor and instructions were also provided, and participants were asked to wear their monitor for 14 d. From days 1–14, the participants collected daily urine samples at home for the DLW assessment, except for 2

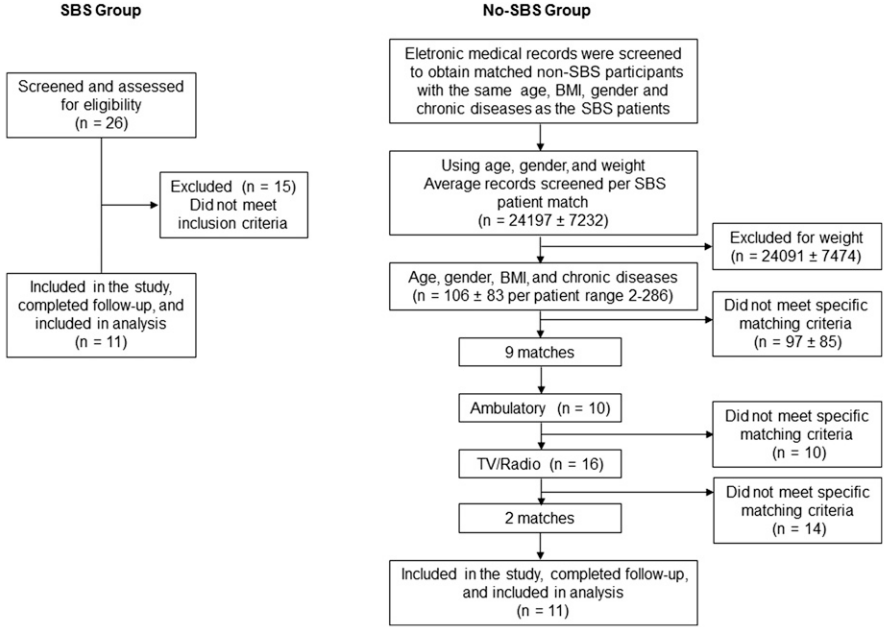

FIGURE 1 Flowchart of participants in the study. SBS and non-SBS participants were matched for similar characteristics, including sex, age, ethnicity, BMI, and chronic diseases, by using a multistage screening process in which thousands of records were screened per patient with SBS to obtain a match. SBS, short bowel syndrome.

TABLE 1
Anthropometric characteristics of the groups[1]

Characteristic	SBS (n = 11)	Non-SBS (n = 11)	P value[2]
Weight, kg	55.7 ± 8.7[3]	57.6 ± 6.6	0.56
Height, cm	161 ± 8	161 ± 7	0.95
BMI, kg/m^2	21.5 ± 3.4	22.3 ± 2.5	0.54
Fat-free mass, kg	42.3 ± 6.6	43.5 ± 5.6	0.64
Fat mass, kg	13.4 ± 3.9	14.2 ± 4.2	0.64
Fat, %	23.7 ± 5.7	24.4 ± 6.6	0.80

[1]Participants without SBS (non-SBS) were matched for characteristics similar to those of patients with SBS, including sex, age, ethnicity, BMI, and chronic diseases. SBS, short bowel syndrome.

[2]Independent Student's t test for comparison between SBS and non-SBS groups.

[3]Mean ± SD (all such values).

participants with SBS who were partial total parenteral nutrition (TPN) and stayed 1 wk at the hospital and 1 wk at home. On day 7, the participants returned to the hospital with the urine samples from their home collection, completed a supervised urine sample collection, and received a recharged replacement of the activity monitor for the remaining 7 d. On day 14, participants provided a day 14 urine sample for the DLW measurement, turned in the last set of home urine collection samples, and returned the activity monitor.

REE

REE was assessed by indirect calorimetry (IC) with the Quark RMR calorimeter (Cosmed). The IC test was conducted during the morning of day 0 after a 12-h fast. Participants were asked to rest quietly in a temperature-controlled room for 30 min before beginning the test. The data acquisition time lasted 30 min using a canopy hood, with the first 5 min omitted from analyses based on standard practice (10, 11). Alcohol burn tests were conducted by using the ethanol-burning kit from Cosmed. Weir's formula (12) was used to calculate energy expenditure from the volume of oxygen consumed and the volume of carbon dioxide produced. Predicted REE was also calculated for each participant by using the Harris-Benedict equation (13) and participants' actual body weight.

Total energy expenditure and estimated energy requirements

Total energy expenditure (TEE) was measured over 14 d by the DLW multipoint method by using the recommendations of the International Dietary Energy Consultancy Group working group (9). After the determination of REE, a baseline urine sample was collected before each participant received a DLW cocktail ($^2H_2{}^{18}O$) (2 g of 10% ^{18}O-labeled and 0.12 g of 99.9% deuterium-labeled water/kg estimated total body water). The deuterium oxide and ^{18}O were supplied by Sercon Ltd. Gateway. Urine samples were collected from days 1–14; daily collections were used to enhance adherence and minimize confusion regarding the "days to collect"; however, only the urine samples from days 1, 2, 3, 7, 12, 13, and 14 were used in the analyses. Measurement of hydrogen and oxygen isotope enrichments was analyzed by using isotope ratio mass spectrometry (Hydra System, ANCA 20–22; Sercon) at the Mass Spectrometry Laboratory in Ribeirão Preto Medical School. TEE was calculated in accordance with the recommendations of the International Dietary Energy Consultancy Group working group (9) by using the method described by Coward (14) and using 0.85 as the assumed value for the respiratory quotient (15).

Energy requirements were estimated for each participant by using the prediction equations of Escott-Stump (6), considering the highest value of kilocalories per kilogram suggested for each range of BMI and compared with the measured TEE.

Anthropometric assessments

At baseline assessment, after an overnight fast and after emptying the bladder, weight was measured to the nearest 100 g (Filizola) with the participant barefoot and wearing light clothing. Height was obtained to the nearest 0.5 cm by using a wall-mounted stadiometer (Filizola). BMI was classified by using the World Health Organization cutoffs (16). Body composition was also assessed with the single-frequency bioelectrical impedance analysis (50 kHz) method by using Biodynamics 450 (Biodynamics Corp.), with the participant in the reclined position, according to recommendations of Kyle et al. (17).

Physical activity

Physical activity level (PAL) was tracked with an activity monitor (activPAL; PAL Technologies) (18). Participants wore the monitor continuously for 24 h/d, over the 14-d period of LW assessment. A fully charged monitor was provided for the first 7 d, after which a newly charged one was provided to complete the remaining 7 d, for a total of 14 d.

The PAL was determined as the ratio between TEE and REE (PAL = TEE:REE), and activity energy expenditure was calculated as (0.9 × TEE) – REE, assuming the diet-induced thermogenesis to be 10% of TEE (19).

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the normality of the data. An independent Student's t test was used to compare the patients with SBS with the non-SBS patients along with a paired Student's t test to compare predicted with

TABLE 2
Energy expenditure of the groups[1]

	SBS (n = 11)	Non-SBS (n = 11)	P value[2]
REE indirect calorimetry, kcal	1357 ± 189[3]	1369 ± 196	0.85
REE Harris-Benedict, kcal	1265 ± 127	1281 ± 104	0.75
TEE DLW, kcal	1875 ± 276	2393 ± 445	0.004
Predicted TEE, kcal	1517 ± 175	1532 ± 178	0.84
Respiratory quotient	0.75 ± 0.06	0.76 ± 0.07	0.78

[1]Participants without SBS (non-SBS) were matched for characteristics similar to those of patients with SBS, including sex, age, ethnicity, BMI, and chronic diseases. DLW, doubly labeled water; REE, resting energy expenditure; SBS, short bowel syndrome; TEE, total energy expenditure.

[2]Independent Student's t test for comparison between SBS and non-SBS groups.

[3]Mean ± SD (all such values).

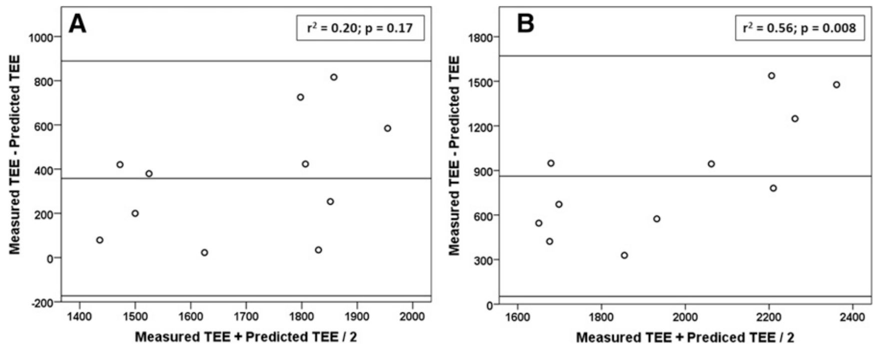

FIGURE 2 Bland-Altman plots for comparison between predicted and measured TEE in the groups with short bowel syndrome (n = 11) (A) and without short bowel syndrome (n = 11) (B). TEE, total energy expenditure.

measured energy expenditure within the same group. Bland-Altman plots were used to compare the predicted TEE with measured TEE energy requirements in each group. The results for TEE and REE were similar with and without the 2 patients with SBS who received partial TPN for some of the time they were on the study (data not shown); therefore, the results are presented with all patients with SBS combined. The significance level used for the tests was set at $P < 0.05$. All analyses were performed by using SPSS Statistics 21.0 (SPSS Inc.).

RESULTS

Participant characteristics

A total of 22 participants, with 11 in each group (5 men and 6 women in each group) aged 37–65 y (mean ± SD: 53 ± 8 y), were evaluated. Participant recruitment and screening are shown in **Figure 1**. The SBS group consisted of 3 participants with SBS due to Crohn disease and 8 individuals with SBS due to mesenteric thrombosis. Mean ± SD time after surgery in the SBS group was 8.2 ± 5.6 y (range: 1–18 y). All patients with SBS had an intestinal transit time of <30 min. Nine of the 11 patients with SBS were from the Ambulatory Nutrition Unit of the University Hospital at the Ribeirão Preto Medical School, and the remaining 2 patients with SBS were from the Metabolic Unit and received partial TPN. These 2 patients were mostly homogeneous to the other 9 non-TPN SBS patients in that they had received the surgical intervention several years prior and received partial TPN only for 1 wk during the 2-wk study period (and even within that 1 wk, energy needs were supported with TPN and oral intake), which required them to be inpatients (although not completely bed bound). Matched non-SBS participants were mostly recruited from the ambulatory nutrition unit of University Hospital of the Ribeirão Preto Medical School (n = 9), and the remaining 2 were recruited from the radio and television announcements because obtaining a match within the hospital records was not possible.

The anthropometric characteristics of the groups are presented in **Table 1**. There were no significant differences in the anthropometric measures between the SBS group and the matched non-SBS controls.

Energy expenditure

Measured and predicted energy expenditure rates are shown in **Table 2**.

REE did not differ significantly between the groups when measured by IC (1357 ± 189 kcal/d, range: 1060–1683 kcal/d, for the SBS group; 1369 ± 196 kcal/d, range: 1099–1705 kcal/d, for non-SBS group) or when predicted by the Harris-Benedict formula (1265 ± 127 kcal/d, range: 1092–1480 kcal/d, for the SBS group; 1281 ± 104 kcal/d, range: 1147–1481 kcal/d, for the non-SBS group). In addition, when the predicted REE was compared with the REE obtained by IC, there was no significant difference between the 2 methods for both the SBS and non-SBS groups (P = 0.06 and P = 0.07, respectively).

TEE measured by the DLW method was significantly lower ($P < 0.01$) in the SBS group (1875 ± 276 kcal/d, range: 1476–2266 kcal/d) than in the non-SBS group (2393 ± 445 kcal/d, range: 1887–3100 kcal/d), whereas predicted TEE did not differ significantly between the SBS group (1517 ± 175 kcal/d, range: 1263–1813 kcal/d) and the non-SBS group (1532 ± 178 kcal/d, range: 1205–1820 kcal/d). However, measured TEE was significantly higher than predicted TEE in both groups (P = 0.001 and $P < 0.01$, respectively, for SBS and non-SBS) (**Figure 2**).

Physical activity

PAL, shown in **Table 3**, was significantly different between the groups, especially for the variables time sitting/lying, time walking, number of steps/d, PAL, and metabolic equivalents, which were higher in the non-SBS group (1.4 metabolic equivalents/h) than in the SBS group (1.75 metabolic equivalents/h).

TABLE 3
Physical characteristics and profile of physical activity of the participants[1]

	SBS (n = 11)	Non-SBS (n = 11)	P value[2]
Time sitting/lying, h	17.6 ± 2.3[3]	15.4 ± 0.8	0.02
Time standing, h	4.9 ± 1.9	6.3 ± 1.4	0.07
Time walking, h	1.5 ± 0.5	2.3 ± 0.8	0.02
Number of steps/d	6632 ± 2302	10,386 ± 3671	0.01
Metabolic equivalents/d	33 ± 1.1	35 ± 1.5	0.01
PAL	1.4 ± 0.1	1.75 ± 0.3	0.001
AEE, kcal	330 ± 177	783 ± 331	0.001

[1]Participants without SBS (non-SBS) were matched for characteristics similar to those of patients with SBS, including sex, age, ethnicity, BMI, and chronic diseases. AEE, activity energy expenditure; PAL, physical activity level; SBS, short bowel syndrome.

[2]Independent Student's t test for comparison between SBS and non-SBS groups.

[3]Mean ± SD (all such values).

DISCUSSION

Nutritional adequacy, particularly the establishment of daily calorie goals, is implicated in playing a critical role both in the postsurgical short-term and longer term prognosis in patients with SBS. However, calorie goals can be successfully met only if the prescription is accurate. To date, there are no objective assessments of the true daily energy needs in patients with SBS. Furthermore, compensation for malabsorptive losses in patients with SBS requires increased intake above the normal daily calorie needs, thus necessitating a better understanding of the actual energy requirements in this patient population.

To our knowledge, our study is the first to objectively measure free-living energy expenditure in patients with SBS, which is one component of energy requirements. Our results show that measured TEE was significantly higher (∼20% for the SBS group and 36% for the non-SBS group) compared with predictions of energy requirements based on age, weight, and sex for this population. In addition, common estimates based on the suggested per kilogram of body weight intake (30–40 kcal/kg/d) also underestimated energy needs in patients with SBS by at least 200–300 kcal/d. Both the SBS and non-SBS groups achieved the goals for the number of walking steps/d goals (6500–8500 steps/d for individuals living with disability or chronic illness and 7000–10,000 steps/d for healthy adults and older adults) (20, 21). However, the overall PALs were significantly lower in our SBS group, and one could speculate that the lack of adequate energy to move around and perform activities of daily life could be a main reason for this lower physical activity profile in these patients. More studies are needed to further investigate these energy expenditure patterns when patients are provided with adequate caloric needs.

Energy requirements of patients with SBS are also influenced by macronutrient malabsorption, because the amount of energy lost in stools is typically 3 times higher in patients with SBS than in healthy participants (22). Furthermore, extensive damage to the digestive system in patients with SBS affects the absorption of nutrients and overall availability of energy for daily function. DiBaise et al. (22) suggest that food intake must be increased by at least 50% of the estimated requirements to compensate for the combined malabsorptive losses in patients with SBS, a factor that can be applied to our new TEE estimates. The authors also suggest that the increased intakes are feasible and best tolerated if consumed throughout the day in 5–6 meal periods (22). Hence, it is important to combine our new information on TEE with realistic estimates for energy losses to compensate for both the high energy requirements of patients with SBS and their malabsorption leading to excessive fecal energy losses (1).

We are somewhat limited in our complete interpretation of estimated additional needs in the patients with SBS because of the lack of a measure of fecal energy losses. Nevertheless, a major strength of this study is the objective measure of free-living energy expenditure by using the DLW method, which provides a comprehensive measure of total energy needs. Because this is the first study to measure TEE by using DLW in patients with SBS, we did not have previous data to estimate a sample size for our study. However, we have included all patients with SBS from São Paulo state who were registered in our hospital records dating back to patients over an 18-y period. Furthermore, because we did observe a significant difference in TEE between SBS and non-SBS participants, it is unlikely that this primary measure in our study was affected by potential sample size limitations.

In contrast, the measured REE in our patients with SBS was not different from those with no SBS. These findings conflict with the data of Araújo et al. (23), who reported a 3% lower measured REE than this study, and Harris-Benedict–predicted REE was also slightly significantly lower. It is important to mention that many of the patients with SBS who were studied by Araújo et al. (23) also participated in this study (participants' medical treatment and care were from the same hospital at the Ribeirão Preto Medical School, São Paulo University). The main differences were that in the previous study, all patients received partial TPN and time elapsed postsurgery was shorter, whereas the same participants who completed our study had more time elapsed postsurgery and were mostly in ambulatory care. These differences may have contributed to the contrasting findings and suggest possible adaptation in REE after a mean surgical time of approximately 8 y. It is also likely that we may not have been adequately powered to detect a difference in longer term REE between our SBS and non-SBS participants. We also calculated predicted REE to examine if there was a significant discrepancy from measured, particularly because predicted REE used in the calculations for estimating TEE may result in the overall underestimation of TEE. Our study shows that this is not the case, and the current prediction equations for REE may be used to obtain a measure of TEE provided the non-REE components are accurately estimated.

In summary, the results from this study show that measured energy requirements in stable, postsurgical patients with SBS are higher by at least 20% over and above what is estimated by prediction equations. Adjustments to the current estimations by increasing energy intake prescriptions in these patients are warranted to support adequate daily energy needs, as well as improve overall quality of life and patient prognosis.

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The authors' responsibilities were as follows—PGF and KP: designed the research; PGF: conducted the research; EF and JSM: provided essential materials and support; PGF, KP, and SKD: analyzed the data; PGF and SKD: wrote the manuscript; and all authors: read and approved the final manuscript and had primary responsibility for the final content. None of the authors declared a conflict of interest.

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