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Hyperphagia in short bowel patients: fat-free mass is a strong predictor

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35

Title

Hyperphagia in short bowel patients: fat-free mass is a strong predictor

Abstract

Background: Some short bowel syndrome patients develop hyperphagic behaviour. Such an increase in food intake stimulates intestinal adaptation and limits dependence on parenteral nutrition. The aim of this study was to determine the factors modulating food consumption in short bowel syndrome patients.

Methods: The associations between oral energy intake and anthropometric, metabolic, nutritional, and intestinal absorption-related characteristics were determined in a monocentric cohort of short bowel syndrome patients on parenteral nutrition with a stable nutritional status. Body composition was assessed by dual X-ray absorptiometry. Data were retrospectively collected from clinical records.

Results: After screening, 38 adult patients with a short bowel syndrome **under parenteral nutrition** ~~and without intestinal transplantation or debilitating gastrointestinal symptoms~~ were included in this study. Oral energy intake ranged from 577 to 4054 kcal per day. Oral energy intake correlated positively with weight, fat-free mass, hand-strength, resting energy expenditure and negatively with free triiodothyronine and C-reactive protein using Spearman correlation. Fat-free mass and thyroid-stimulating hormone remained positively correlated with oral energy intake independently of all other parameters in a multilinear regression model.

Conclusions: Fat-free mass is a strong predictor of oral energy intake in short bowel syndrome patients **under parenteral nutrition and without debilitating gastrointestinal symptoms**. Increasing fat-free mass ~~using a physical activity program~~ could be a way to

BMI, body mass index, CRP, C-reactive protein, DEXA, dual X-ray absorptiometry, FFM, fat-free mass, FFMI, fat-free mass index, FM, fat mass, FMI, fat mass index, FT3, free triiodothyronine, FT4, free thyroxine, REE, resting energy expenditure, TSH, thyroid-stimulating hormone

25 stimulate oral energy intake in short bowel syndrome patients. This assumption should be
26 assessed by further studies.

27

28 *Keywords:* parenteral nutrition; energy metabolism; body composition; fat-free mass;
29 thyrotropin; intestinal absorption

30 **Introduction**

31 In adults, short bowel syndrome is secondary to intestinal resection for gastrointestinal
32 conditions including mesenteric ischemia, inflammatory bowel diseases, occlusive syndromes
33 or bowel cancers. This syndrome is defined by a remnant bowel length inferior to 150-200
34 cm. Massive small intestine resection induces temporary or permanent intestinal failure owing
35 to malabsorption related to a reduced intestinal surface ¹.

36 The development of parenteral nutrition during the last decades has changed the prognosis
37 of short bowel syndrome patients. However, long-term parenteral nutrition induces serious
38 complications, e.g., central venous catheter-related bloodstream infections and intestinal
39 failure-associated liver disease ^{2,3}. Moreover, home parenteral nutrition is an expensive
40 treatment associated with a poor quality of life ^{4,5}. Thus, one of the main objectives of short
41 bowel syndrome patient care is to promote intestinal adaptation and to reduce dependence on
42 parenteral nutrition. Some short bowel syndrome patients present adaptive hyperphagia which
43 is critical for intestinal adaptation ^{6,7}. Stimulating food consumption could therefore be a safe
44 and inexpensive way to reduce dependence on parenteral nutrition ⁸.

45 Few studies have assessed the factors which modulate oral energy intake in short bowel
46 syndrome patients. These studies focused on the links between hyperphagia and certain
47 hormones – namely leptin, dipeptidyl peptidase-4, peptide YY and ghrelin, with inconclusive
48 results ⁹⁻¹¹. Since fat-free mass correlates with oral energy intake in healthy normal weight
49 and obese subjects, we hypothesised that body composition could at least partly determine
50 oral energy intake in short bowel syndrome patients ¹²⁻¹⁴. The aim of our study was to
51 determine the factors associated with oral energy intake in short bowel syndrome patients on
52 home parenteral nutrition and stable nutritional status.

53 **Materials and Methods**

54 **Study population**

55 This study was based on observational routinely-collected data from one home
56 parenteral nutrition referral centre in Lyon, France. Health data were recorded in
57 computerised patient records during clinical practice. In our centre, every patient, who is
58 under home parenteral nutrition for extended period, is routinely hospitalised for nutritional
59 assessment. All short bowel subjects, who were hospitalised for a nutritional this assessment
60 in our unit from January 2007 to October 2016 were screened. Clinically stable patients with a
61 short bowel syndrome for at least 1 year and on home parenteral nutrition were included.
62 Short bowel syndrome was defined as a remnant short bowel length inferior to 200 cm with or
63 without colon resection ¹. Owing to the eating difficulties of adult patients with a paediatric
64 short bowel syndrome, these patients were excluded from our study ¹⁵. Patients with intestinal
65 transplantation, and those with an oral energy intake below 500 kcal and/or frequent
66 nausea/vomiting were also excluded.

67 **Nutritional assessment**

68 All included patients received a standardised nutritional assessment during a hospital
69 stay of a few days. If a patient received several nutritional assessments, only the data from the
70 most recent hospitalisation were collected. These nutritional assessments are routinely
71 performed in the home parenteral nutrition referral centre of Lyon. The purpose is to ensure
72 that the long-term home parenteral nutrition is appropriate. Nutritional assessment includes
73 body composition analysis and anthropometry, a 3-day food diary, indirect calorimetry, blood
74 and stool tests.

75 **Body composition and anthropometry**

All anthropometric measurements were performed by medical practitioners. Weight, height, brachial circumference at the centre of the upper limb and triceps skinfold at the same site using an anthropometric calliper were determined. The device used for determination of handgrip strength changed in 2012. Thus, only handgrip strength measured with a Jamar dynamometer data after 2012 was considered. Fat-free mass and fat mass were estimated by dual X-ray absorptiometry (DEXA). Indirect calorimetry (Quark RMR – Cosmed) was performed for 30 min in fasting subjects after discontinuation of parenteral nutrition for at least six hours.

Determination of food intake and definition of hyperphagia

Oral energy intake was assessed by a trained dietitian using a 3-day food diary filled out at home prior to hospitalisation.

Some authors have attempted to define hyperphagia in short bowel syndrome but no clear definition has yet to emerge. Based on a review of the literature, two principal definitions have been retained in this paper in order to classify the subjects as hyperphagic or non-hyperphagic. We defined subjects as hyperphagic if they had an oral energy intake greater than either $40 \text{ kcal.kg}^{-1}.\text{day}^{-1}$ ⁹ or one and a half times their resting energy expenditure⁶.

Blood and stool tests

Blood tests were performed including determination of albuminemia, C-reactive protein (CRP) level, thyroid function, and plasma amino acids in order to measure plasma citrulline concentration. Intestinal carbohydrate absorption was determined using a blood D-xylose test. Fasting subjects were given 5g of D-xylose dissolved in 200 mL water and D-xylose blood concentration was measured after one hour. Stools were collected by subjects for three days at home before hospitalisation in order to determine average daily stool weight.

Ethics statement

According to current French law, patients were individually informed that their data could be used for research (MR-003 reference methodology) and did not object. Data were collected during routine medical examination. Patients did not undergo any treatment or examination specifically devised to collect data for this study.

Statistical analysis

Statistical analysis was performed using RStudio Version 1.0.136 with occasional reliance on ‘prettyR’, ‘RVAideMemoire’, ‘ggplot2’, ‘car’, ‘zoo’¹⁶. Owing to the small number of patients, non-parametric statistics were used. Data are presented as median and 95% confidence interval. All P-values below 0.05 were considered significant.

The relationship between oral energy intake and the following 24 variables were examined: age, sex, short bowel syndrome causes, bowel anatomy, remnant small bowel length, duration of short bowel syndrome, resting energy expenditure, body weight, fat-free mass, fat mass, brachial circumference, skinfold, hand strength, plasma albumin, thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), CRP, parenteral energy intake, number of parenteral infusions per week, volume of parenteral infusion stool weight, one-hour D-xylose blood concentration and citrullinemia. In order to determine the predictive factors of oral energy intake, a univariate analysis was first completed using Spearman correlations and Wilcoxon-Mann-Whitney test or Kruskal-Wallis test for categorical variables with more than two factors. For the Spearman correlation determination, the results were expressed as Rho and 95% confidence interval. Confidence intervals were determined using a bootstrap with 1000 replicates.

Subsequently, a multiple regression analysis was performed to determine the factors significantly and independently associated with oral energy intake. Variables with P-value

124 below 0.1 in univariate analyses as well as age and sex were entered. Hand-strength was
125 excluded because too many values were missing. Owing to the collinearity between weight
126 and fat-free mass, assessed by variance influence factor, weight was replaced by fat mass.
127 Variance influence factor was below 5 for each factor after this adjustment. The residual of
128 multiple linear regression was normally distributed using the Shapiro-Wilk test ¹⁷.

129 **Results**

130 **Patient inclusion**

131 All patients (n = 119) on home parenteral nutrition and hospitalised for a nutritional
132 assessment between January 2007 and October 2016 were screened (Figure 1). A total of 38
133 patients were included.

Figure 1. Patient inclusion flowchart.

SBS, short bowel syndrome, DEXA, Dual-energy X-ray absorptiometry

137 **Patient characteristics**

138 The study population was made up of 24 males (63%) and 14 females with a median
139 age of 63 years [IC95%: 37-77]. Patients underwent intestinal resection due to mesenteric
140 ischaemia (n=24, 63%), small bowel obstruction (n=5, 13%), intestinal tumour (n=3, 8%),
141 radiation enteritis (n=3, 8%), or other causes (n=3, 8%). The median remnant small bowel
142 length was 70 cm [IC95%: 8-164]. Among the 18 patients with a stoma, 16 patients had an
143 end-jejunostomy while 2 had a colostomy with a jejuno-colic anastomosis. Among the 20
144 patients without a stoma, 17 had a jejuno-colic anastomosis and 3 a jejuno-ileal anastomosis.
145 The median period between nutritional assessment and bowel resection was 52 months
146 [IC95%: 16-214]. Table 1 shows the demographic, anthropometric, metabolic, nutritional and
147 intestinal absorption-related characteristics.

	Median [IC 95%]
age, years, n = 38	63 [37, 77]
sex, %, (M/F), n = 38	63% (24/14)
<i>Anthropometric characteristics</i>	
body weight, kg, n = 38	63.0 [48.9, 80.0]
BMI, kg.m-2, n = 38	22.0 [17.3, 26.8]
FFM, kg, n = 38	42.9 [34.9, 58.2]
FFMI, kg.m-2, n = 38	15.5 [13.4, 19.5]
FM, kg, n = 38	16.5 [7.9, 28.3]
FMI, kg.m-2, n = 38	6.2 [2.7, 11.0]
brachial circumference, cm, n = 35	27 [23, 34]
skinfold, mm, n = 35	14 [5, 33]
Hand strength, kg, n = 14	32 [17, 43]
<i>Metabolic characteristics</i>	
REE, kcal, n = 37	1394 [1053, 1685]
TSH, mUI/L, n = 36	1.29 [0.48, 3.07]
FT3, pmol/L, n = 35	4.1 [3.3, 5.2]
FT4, pmol/L, n = 35	12.8 [10.1, 17.3]
CRP, mg/L, n=38	3.3 [0.9, 15.7]
albumin, g/L, n = 38	37.3 [28.1, 44.0]
<i>Nutritional characteristics</i>	
oral energy intake, kcal/d, n = 38	2087 [1293, 3586]
parenteral energy intake, kcal/d, n = 38	840 [286, 1682]
number of parenteral infusions, per week, n = 38	4 [2, 7]
volume of parenteral infusion, L, per bag, n = 38	1142 [286, 3038]
amino acid content of parenteral infusion, g/kg/day, per bag, n = 38	0.62 [0.24, 1.22] g/kg/day
<i>Intestinal absorption-related characteristics</i>	
stool weight, g per day, n = 35	1165 [186, 2939]
one-hour D-xylose blood concentration, mmol/L, n = 31	0.60 [0.24, 1.51]
citrullinemia, mmol/L, n = 38	20 [7, 43]

148 Table 1. Anthropometric, metabolic, nutritional and intestinal absorption-related
149 characteristics of the population.

150 BMI, body mass index, FFM, fat-free mass, FFMI, fat-free mass index, FM, fat mass, FMI,
151 fat mass index REE, resting energy expenditure, TSH, thyroid-stimulating hormone, FT3, free
152 triiodothyronine, FT4, free thyroxine, CRP, C-reactive protein

Oral and parenteral energy intake

Patients were assigned either to the hyperphagic or the non-hyperphagic group according to the two retained hyperphagia definitions, namely an oral energy intake greater than $40 \text{ kcal.kg}^{-1}.\text{day}^{-1}$ (Figure 2A) or one and a half times their resting energy expenditure (Figure 2B). Subjects with hyperphagia accounted for 26% (n=10) using the first definition (Figure 2A) and 43% (n=16) using the second definition (Figure 2B). As illustrated in Figures 2A and 2B, oral energy intake had a Gaussian distribution which did not make it possible to clearly distinguish the group of hyperphagic patients from the group of non-hyperphagic patients. Whatever the definition of hyperphagia, the hyperphagic patients were only the patients with the greatest energy intake (on the right of the curve). Given this and for further analyses, the population was analysed as a whole. Oral and parenteral energy intake and resting energy expenditure for each patient are given in Figure 2C. In the vast majority of cases, oral energy intake provided more than resting energy needs.

Figure 2. Oral energy intake (OEI), parenteral energy intake (PEI) and resting energy expenditure (REE) in the cohort of 38 short bowel syndrome patients

A. Distribution of the OEI in patients designated either non-hyperphagic ($\text{OEI/weight} < 40 \text{ kcal.kg}^{-1}.\text{day}^{-1}$, $n = 28$, 73.7%) or hyperphagic patients ($\text{OEI/weight} \geq 40 \text{ kcal.kg}^{-1}.\text{day}^{-1}$, $n=10$, 26.3%)

B. Distribution of the OEI in patients designated either non-hyperphagic ($\text{OEI} < 1.5 \times \text{REE}$, $n=21$, 56.8%) or hyperphagic patients ($\text{OEI} \geq 1.5 \times \text{REE}$, $n=16$, 43.2%)

C. Individual variations of parenteral energy intake (PEI), oral energy intake (OEI) and resting energy expenditure (REE). The subjects were ranked according to their oral energy intake. OEI is marked in dark grey if patients are hyperphagic with either of the two definitions.

One subject was not represented in Figure 2B and 2C because the REE was missing.

Relationship between oral energy intake and characteristics of the population and parenteral intake

Significant univariate analyses are illustrated in Figure 3. Oral energy intake was correlated with weight ($Rho = 0.418$ [0.095, 0.684], $P = 0.009$), fat-free mass ($Rho = 0.474$ [0.158, 0.699], $P = 0.003$) but not with fat mass ($Rho = 0.021$ [-0.313, 0.337], $P = 0.90$). Despite the low numbers of subjects with a measure of hand strength ($n = 14$), oral energy intake was significantly correlated with hand strength ($Rho = 0.585$ [0.053, 0.869]). Oral energy intake was also positively correlated with resting energy expenditure ($Rho = 0.365$ [0.042, 0.628], $P = 0.03$) and negatively correlated with FT3 ($Rho = -0.346$ [-0.622, -0.031], $P = 0.04$) and CRP ($Rho = -0.360$ [-0.625, -0.027] (Figure 3). Oral energy intake was not correlated with any other parameters including age, mean remnant small bowel length, short bowel syndrome duration, parameters related to parenteral nutrition and intestinal functions (Table 2). The oral energy intake in subgroups of patients categorised by sex, short bowel syndrome causes and bowel anatomy was not significantly different ($P = 0.11$, $P = 0.97$, $P = 0.88$ respectively). Using multiple linear regression analysis with oral energy intake as the dependent variable, and with age, sex, fat-free mass, resting energy expenditure, TSH, FT3 and CRP as independent variables, oral energy intake positively correlated with fat-free mass ($P < 0.05$) and TSH ($P < 0.01$) independently of all other parameters (Table 3).

197

198 Figure 3. Significant associations between oral energy intake (OEI) and body weight, resting
 199 energy expenditure (REE), fat-free mass (FFM), hand strength, free triiodothyronine (FT3),
 200 and C-reactive protein (CRP).

201 Univariate associations were assessed using Spearman correlations. The confidence interval
 202 of the Spearman correlation coefficients was determined using a bootstrap with 1000
 203 replicates.

204 Hyperphagic patients with either of the two definitions are marked in dark grey and non-
205 hyperphagic patients are marked in light grey.

	Rho	IC95	p
age, years	-0.051	[-0.385, 0.288]	0.76
FM, kg	0.021	[-0.313, 0.337]	0.90
brachial circumference, cm	0.065	[-0.322, 0.401]	0.71
skinfold, mm	-0.169	[-0.511, 0.213]	0.33
TSH, mUI/L	0.322	[-0.002, 0.621]	0.06
FT4, pmol/L	-0.204	[-0.503, 0.146]	0.24
parenteral energy intake, kcal/d	0.154	[-0.175, 0.486]	0.36
number of parenteral infusions, per week	0.098	[-0.263, 0.421]	0.56
volume of parenteral infusion, L, per bag	0.129	[-0.217, 0.448]	0.44
albumin, g/L	0.144	[-0.213, 0.475]	0.39
duration of the short bowel syndrome, months	-0.022	[-0.367, 0.317]	0.90
remnant small bowel length, cm	-0.010	[-0.366, 0.344]	0.95
stool weight, g	0.050	[-0.340, 0.395]	0.77
one-hour blood D-xylose concentration, mmol/L	0.112	[-0.246, 0.434]	0.55
citrullinemia, mmol/L, n = 38	0.094	[-0.220, 0.408]	0.57

207 Table 2. Correlation between oral energy intake and anthropometric, metabolic, nutritional
 208 and absorption parameters using Spearman's rank correlation
 209 IC 95% was determined after bootstrap with 1000 replicates.
 210 FM, fat mass, TSH, thyroid-stimulating hormone, FT4, free thyroxine

Predictor variables	β (Standardised coefficients)	Standard error	P-value
sex	-0.206	0.14	0.30
age	0.103	0.17	0.44
FFM	0.660	0.44	<0.01
FM	0.187	0.11	0.18
REE	0.307	0.40	0.12
TSH	0.398	0.05	<0.01
FT3	-0.044	0.29	0.74
CRP	-0.054	0.05	0.68

211 Table 3. Multivariate model with oral energy intake as the dependent variable and predictor
212 variables as the independent variables.
213 FFM, fat-free mass, FM, fat mass, REE, resting energy expenditure, TSH, thyroid-stimulating
214 hormone, FT3, free triiodothyronine

215 **Discussion**

216 ~~In short bowel syndrome patients, the development of hyperphagia is essential for~~
217 ~~intestinal adaptation and subsequently to reduce dependence on parenteral nutrition.~~ In short
218 bowel syndrome patients, luminal nutrients are essential for intestinal adaptation and
219 hyperphagia can reduce dependence on parenteral nutrition in some patients. Despite much
220 interest in this area, previous studies have failed to determine the factors that explain the
221 increase in food consumption in some short bowel syndrome patients.

222 In this observational study, we reported the correlations between oral energy intake
223 and the factors potentially involved in oral energy intake in these patients. The most striking
224 result is that oral energy intake strongly correlated with fat-free mass, both in linear and
225 multiple linear regression models. We hypothesise that fat-free mass drives oral energy intake
226 in short bowel syndrome patients. However, one may argue that in short bowel syndrome
227 patients, greater oral energy intake induces a better nutritional status leading to greater fat-free
228 mass. This hypothesis is unlikely since the correlation between fat-free mass and oral energy
229 intake is shared across many different populations, i.e. healthy normal weight, overweight or
230 obese adults and adolescents who are not expected to be malnourished^{12–14,18–20}. Furthermore,
231 all of the patients in our cohort were thoroughly monitored before their nutritional assessment
232 and the parenteral nutrition was periodically adjusted to maintain a satisfactory nutritional
233 status. A difference in nutritional status within the cohort was therefore not expected. We also
234 found a positive correlation between TSH and oral energy intake in the multivariate model.
235 One possible explanation for this result is that the subjects with the highest oral energy intake
236 tend to be overfed. Indeed, an increase in TSH was previously demonstrated in response to
237 experimental overfeeding²¹.

238 In order to understand the drivers of oral energy intake, one important and
239 controversial issue was to know if parenteral nutrition inhibits oral intake. In our study, oral

energy intake was not correlated with any parameter related to parenteral nutrition, namely energy, number and volume of infusions in good agreement with other observational studies^{6,22}. It is also reinforced by experimental studies showing the lack of acute effect of parenteral nutrition on hunger and satiety both in short bowel syndrome patients²³ and healthy subjects²⁴ even if some other studies suggest an effect of parenteral nutrition on subsequent oral energy intake^{25,26}. Our results also showed that the duration of short bowel syndrome is not associated with oral energy intake at least in the included patients, which are on parental nutrition for at least one year.

The main limitation of our study is its retrospective design. This limitation is related to the difficulty of collecting prospective data in short bowel syndrome patients owing to the low population size. To limit the bias of recruitment and ensure consecutive recruitment during the study period, we screened all patients with a nutritional assessment in our unit. We analysed only fat-free mass data assessed by DEXA to ensure the homogeneity of the results. Oral energy intake determination was based on a 3-day diary and one concern is therefore possible misreporting of oral energy intake. Nevertheless, good agreement between objective and subjective assessment of oral energy intake in the short bowel syndrome population has been previously shown⁷. Finally, we excluded patients with limited oral energy intake and/or frequent nausea/vomiting. In our retrospective study, these gastrointestinal symptoms were not precisely quantified. Thus, we were not able to include them in statistical analyses and to determinate in which measure they affect oral energy intake.

This study has revealed that fat-free mass is an important determinant of oral energy intake. One way to increase fat-free mass could be to increase physical activity. Such a strategy was previously assessed with a resistance training program inducing an increase in both fat-free mass and energy intake in nine short bowel patients²⁷. This study is promising

and should be validated in a larger cohort. Future work should also assess, if increasing fat-free mass limits dependence on parenteral nutrition

In conclusion, our work suggests that fat-free mass is an important determinant of oral energy intake in short bowel syndrome patients under parenteral nutrition and without debilitating digestive symptoms. This finding adds to a body of evidence highlighting the correlation of fat-free mass and oral energy intake in other populations. Future studies are therefore required to elucidate the links between oral energy intake, fat-free mass, physical activity and dependence on parenteral nutrition in short bowel syndrome patients. It could help to better follow up these patients in order to ensure both intestinal adaptation and nutritional adequacy.

References

1. Pironi L, Arends J, Baxter J, et al. ESPEN endorsed recommendations. Definition and classification of intestinal failure in adults. *Clin Nutr*. 2015;34(2):171-180. doi:10.1016/j.clnu.2014.08.017.
2. Dibb M, Soop M, Teubner A, et al. Survival and nutritional dependence on home parenteral nutrition: Three decades of experience from a single referral centre. *Clin Nutr Edinb Scotl*. 2017;36(2):570-576. doi:10.1016/j.clnu.2016.01.028.
3. Santarpia L, Buonomo A, Pagano MC, et al. Central venous catheter related bloodstream infections in adult patients on home parenteral nutrition: Prevalence, predictive factors, therapeutic outcome. *Clin Nutr Edinb Scotl*. 2016;35(6):1394-1398. doi:10.1016/j.clnu.2016.03.009.
4. Berghöfer P, Fragkos KC, Baxter JP, et al. Development and validation of the disease-specific Short Bowel Syndrome-Quality of Life (SBS-QoLTM) scale. *Clin Nutr Edinb Scotl*. 2013;32(5):789-796. doi:10.1016/j.clnu.2012.12.001.
5. Roskott AM, Groen H, Rings EHHM, et al. Cost-effectiveness of intestinal transplantation for adult patients with intestinal failure: a simulation study. *Am J Clin Nutr*. 2015;101(1):79-86. doi:10.3945/ajcn.114.083303.
6. Crenn P, Morin MC, Joly F, Penven S, Thuillier F, Messing B. Net digestive absorption and adaptive hyperphagia in adult short bowel patients. *Gut*. 2004;53(9):1279-1286. doi:10.1136/gut.2003.030601.
7. Messing B, Pigot F, Rongier M, Morin MC, Ndeïndoum U, Rambaud JC. Intestinal absorption of free oral hyperalimentation in the very short bowel syndrome. *Gastroenterology*. 1991;100(6):1502-1508.

- 297 8. Amiot A, Messing B, Corcos O, Panis Y, Joly F. Determinants of home parenteral
298 nutrition dependence and survival of 268 patients with non-malignant short bowel
299 syndrome. *Clin Nutr Edinb Scotl*. 2013;32(3):368-374. doi:10.1016/j.clnu.2012.08.007.
- 300 9. Compher CW, Kinosian BP, Metz DC. Ghrelin does not predict adaptive hyperphagia in
301 patients with short bowel syndrome. *JPEN J Parenter Enteral Nutr*. 2009;33(4):428-
302 432. doi:10.1177/0148607108324583.
- 303 10. Molina A, Pita A, Farriol M, Virgili N, Soler J, Gómez JM. Serum leptin concentrations
304 in patients with short-bowel syndrome. *Clin Nutr Edinb Scotl*. 2000;19(5):333-338.
305 doi:10.1054/clnu.2000.0110.
- 306 11. Farriol M, Pita AM, Fernandez-Bustos MA, Delgado G. Dipeptidyl-peptidase IV in
307 patients with short bowel syndrome. *Clin Nutr Edinb Scotl*. 2005;24(6):1099-1104.
308 doi:10.1016/j.clnu.2005.07.001.
- 309 12. Blundell JE, Caudwell P, Gibbons C, et al. Body composition and appetite: fat-free mass
310 (but not fat mass or BMI) is positively associated with self-determined meal size and
311 daily energy intake in humans. *Br J Nutr*. 2012;107(3):445-449.
312 doi:10.1017/S0007114511003138.
- 313 13. Lissner L, Habicht JP, Strupp BJ, Levitsky DA, Haas JD, Roe DA. Body composition
314 and energy intake: do overweight women overeat and underreport? *Am J Clin Nutr*.
315 1989;49(2):320-325.
- 316 14. Weise CM, Hohenadel MG, Krakoff J, Votruba SB. Body composition and energy
317 expenditure predict ad-libitum food and macronutrient intake in humans. *Int J Obes*
318 2005. 2014;38(2):243-251. doi:10.1038/ijo.2013.85.

- 319 15. Senez C, Guys JM, Mancini J, Paz Paredes A, Lena G, Choux M. Weaning children
320 from tube to oral feeding. *Childs Nerv Syst ChNS Off J Int Soc Pediatr Neurosurg*.
321 1996;12(10):590-594.
- 322 16. RStudio Team. *RStudio: Integrated Development Environment for R*. Boston, MA:
323 RStudio, Inc.; 2016.
- 324 17. Royston JP. Algorithm AS 181: The W Test for Normality. *J R Stat Soc Ser C Appl Stat*.
325 1982;31(2):176-180. doi:10.2307/2347986.
- 326 18. Hopkins M, Finlayson G, Duarte C, et al. Modelling the associations between fat-free
327 mass, resting metabolic rate and energy intake in the context of total energy balance. *Int*
328 *J Obes*. 2016;40(2):312-318. doi:10.1038/ijo.2015.155.
- 329 19. Vainik U, Konstabel K, Lätt E, Mäestu J, Purge P, Jürimäe J. Diet misreporting can be
330 corrected: confirmation of the association between energy intake and fat-free mass in
331 adolescents. *Br J Nutr*. 2016;116(8):1425-1436. doi:10.1017/S0007114516003317.
- 332 20. Cameron JD, Sigal RJ, Kenny GP, et al. Body composition and energy intake - skeletal
333 muscle mass is the strongest predictor of food intake in obese adolescents: The
334 HEARTY trial. *Appl Physiol Nutr Metab Physiol Appl Nutr Metab*. 2016;41(6):611-617.
335 doi:10.1139/apnm-2015-0479.
- 336 21. Oppert JM, Dussault JH, Tremblay A, Després JP, Thériault G, Bouchard C. Thyroid
337 hormones and thyrotropin variations during long term overfeeding in identical twins. *J*
338 *Clin Endocrinol Metab*. 1994;79(2):547-553. doi:10.1210/jcem.79.2.8045975.
- 339 22. Fernández-Estívariz C, Luo M, Umeakunne K, et al. Nutrient Intake From Habitual Oral
340 Diet in Patients With Severe Short Bowel Syndrome Living in the Southeastern United

- 341 States. *Nutr Burbank Los Angel Cty Calif*. 2008;24(4):330-339.
342 doi:10.1016/j.nut.2007.12.016.
- 343 23. Murray CD, le Roux CW, Gouveia C, et al. The effect of different macronutrient
344 infusions on appetite, ghrelin and peptide YY in parenterally fed patients. *Clin Nutr*.
345 2006;25(4):626-633. doi:10.1016/j.clnu.2005.12.002.
- 346 24. Borer KT, Wuorinen E, Ku K, Burant C. Appetite Responds to Changes in Meal
347 Content, Whereas Ghrelin, Leptin, and Insulin Track Changes in Energy Availability. *J*
348 *Clin Endocrinol Metab*. 2009;94(7):2290-2298. doi:10.1210/jc.2008-2495.
- 349 25. Gil KM, Skeie B, Kvetan V, Askanazi J, Friedman MI. Parenteral Nutrition and Oral
350 Intake: Effect of Glucose and Fat Infusions. *J Parenter Enter Nutr*. 1991;15(4):426-432.
351 doi:10.1177/0148607191015004426.
- 352 26. Sriram K, Pinchcofsky G, Kaminski MV. Suppression of appetite by parenteral nutrition
353 in humans. *J Am Coll Nutr*. 1984;3(4):317-323.
- 354 27. Araújo ECF, Suen VMM, Marchini JS, Vannucchi H. Muscle mass gain observed in
355 patients with short bowel syndrome subjected to resistance training. *Nutr Res*.
356 2008;28(2):78-82. doi:10.1016/j.nutres.2007.12.007.
- 357