The Impact of Laparoscopic Sleeve Gastrectomy on Serum Zinc or Copper and Body Composition

DANIEL TIMOFTE[1], LACRAMIOARA OCHIUZ[2]*, MANUELA URSARU[1], BOGDAN CIUNTU[3], LIDIA IONESCU[1], VALENTIN CALU[4], VERONICA MOCANU[5], ION COSMIN PUIA[6,7]

[1] Grigore T. Popa University of Medicine and Pharmacy, Department of General Surgery, 16 Universitatii Str., 700115, Iasi, Romania

[2] Grigore T. Popa University of Medicine and Pharmacy, Department of Pharmaceutical and Biotechnological Drug Industry, 16 Universitatii Str., 700115, Iasi, Romania

[3] Grigore T. Popa University of Medicine and Pharmacy, Department of Radiology, 16 Universitatii Str. , 700115, Iasi, Romania

[4] Carol Davila University of Medicine and Pharmacy, Department of General Surgery, Elias Emergency University Hospital, 37 Dionisie Lupu Str., 030167 Bucharest, Romania

[5] Grigore T. Popa University of Medicine and Pharmacy, Department of Pathophysiology, 16 Universitatii Str., 700115, Iasi, Romania

[6] Iuliu Hateganu University of Medicine and Pharmacy, 8 Victor Babes Str., 400000 Cluj Napoca, Romania

[7]Octavian Fodor Regional Institute of Gastroenterology and Hepatology of Cluj Napoca, 19 Croitorilor Str., 400000, Cluj Napoca, Romania

The aim of this study was to investigate the impact of bariatric surgery on body composition, serum zinc and serum copper levels in obese patients over a period of 12 months following laparoscopic sleeve gastrectomy. This could be important considering that this procedure has been proven to be an effective tool in achieving absolute weight loss and reducing fat tissue in morbidly obese population. Thus, our present results are confirming some important modifications behind the biochemistry of the bariatric surgery and the aforementioned impact of laparoscopic sleeve gastrectomy on serum zinc or copper and body composition.

Keywords: zinc, copper, serum, bariatric, gastrectomy

Bariatric surgery is widely accepted as the most effective strategy leading to long-term weight loss. The results of this operation are impressive: studies have shown a decrease in mortality, in cardiovascular events and cancer incidence [1, 2]. Furthermore, it has been observed a major improvement in metabolic obesity-related comorbidities [3–5], as our group and others also previously described on various levels, related areas of research and experimental designs and [6-15].

However, how much fat mass (FM) or muscle mass (MM) is lost, is still uncertain. In the ideal case, there would be an expectation of significant loss of body fat and a desired limited loss of muscle tissue. In the event that an excessive loss of lean body mass (LBM) occurs, certain metabolic consequences are expected, due to LBM being a key determinant of weight loss and also to glycemic regulation. Furthermore, a significant loss of muscle mass (MM) in particular, may lead to a poorer quality of life, with an occurrence of functional impairment due to an accelerated onset of fatigue in daily activities. In addition, muscle tissue is a major determinant of insulin sensitivity, and also involved in post-prandial glucose disposal. Other studies have shown that the percentage of lean body mass lost after bariatric surgery is expected to be approximately 31% of the total mass lost [16-21].

It is well documented that obese individuals experience chronic inflammation resembling that found in various infectious disease [22, 23]. It seems likely that zinc and copper metabolism are altered similarly by cytokines [24] and signaling pathways [22, 25] in infection and obesity. However, it is not certain that the quality and the quantity of inflammation are identical in both of these conditions. The response to acute and chronic inflammation is described as a number of plasma proteins, such as ceruloplasmin, being synthesized in liver under the influence of cytokines and secreted into the circulation [13]. Furthermore, a few other proteins, such as albumin, present a simultaneous decrease. Some of the albumin decline presented in the literature may have resulted from inflammation. It is well known that albumin is the principal zinc-binding protein [26] in serum. Therefore, with lower albumin, there are fewer binding sites for zinc. Consequently, the zinc deficiencies observed in obese populations may be due to cytokine effects on albumin.

However, low values for serum copper are relatively rare in the literature [23]. But some author suggest that even if a copper deficiency was to be present, diagnosis may have been masked by cytokine effects that increased serum copper values because ceruloplasmin is the predominant carrier of circulating copper [27]. Perhaps copper deficiency would have been found if patients had been evaluated with some of the newer, potentially more sensitive, indices of copper status such as erythrocyte and extracellular superoxide dismutases, leukocyte copper, platelet cytochrome c oxidase or serum lysyl oxidase [28–32].

Although the Western diet, for example, is often low in copper [33, 34], copper deficiency has not been described in patients before bariatric surgery. However, a copper deficiency is often reported after bariatric surgeries [35–37].

Studies in the literature show that patients who undergo laparoscopic sleeve gastrectomy show a 65% to 80% loss in body weight over a 12- to 18-month postoperative follow up [38, 39], but there are relatively few studies that present how much of this is muscle mass or fat mass. These changes are the result of a calorie deficit, low protein intake, and quick weight loss, with patients who undergo bariatric

* email: ochiuzd@yahoo.com

Table 1
CHARACTERISTICS OF STUDY PARTICIPANTS BEFORE AND 12 MONTHS AFTER LAPAROSCOPIC SLEEVE GASTRECTOMY. DATA ARE PRESENTED AS MEAN (SD)

	Before surgery		P	After 12 months		P
	Experimental group	Control group		Experimental group	Control group	
Age (years)	40.23(6.8)	42 (7.6)	0.088	-	-	
Gender (M/F)	44/46	33/56	-			
Body composition analysis						
Weight (kg)	122.1(18.3)	120.6 (20)	0.605	-	-	
Height (cm)	171 (9.2)	169.6 (7.1)	0.275	-	-	
Lean body mass (kg)	57.2(10.9)	57.1 (10.9)	0.965	47.2 (10.8)	57.2 (10.8)	<0.001
Fat mass (kg)	56.8 (10.9)	56.7 (10.9)	0.961	30.6 (10.4)	56.8 (10.8)	<0.001
Muscle mass (kg)	25.5 (10.6)	25.4 (10.6)	0.963	20.6 (9.7)	25.4 (10.5)	0.002
Biochemical variables						
Serum zinc (ug/dl)	77.3 (8.7)	77.1 (12.6)	0.897	63 (11.1)	76.6 (12.6)	<0.001
Serum copper (ug/dl)	147(11)	147.1 (16.8)	0.966	90.2 (14.7)	147.6 (16.9)	<0.001

surgery likely to see changes in body composition over the course of treatment. The aim of this study was to investigate the impact this procedure has on body composition, serum zinc and serum copper levels in obese patients over a period of 12 months following laparoscopic sleeve gastrectomy.

Experimental part

Participants

90 patients (44 men and 46 women), all Romanians, who were hospitalized for laparoscopic sleeve gastrectomy surgery in the Surgery Service, Sf. Spiridon Clinical Emergency Hospital in Iasi (Romania) were recruited to be part of the experimental group. These patients were investigated before and 12 months after the laparoscopic sleeve gastrectomy. Data from the experimental group was compared to that of a control group, recruited from the waiting list for laparoscopic sleeve gastrectomy, consisting of 89 patients, 33 males and 56 females. The control group was recruited to match weight, lean body mass, fat mass, muscle mass, serum zinc and serum copper in relation to the corresponding baseline values in the group who underwent laparoscopic sleeve gastrectomy, as it can be seen in table 1.

All patients signed a specific study inclusion agreement annexed to the informed consent form [40], and all experimental biochemical studies were performed in the light of the uniformly accepted ethical principles stated by the Helsinki Declaration [41-47].

Body composition analysis

Weight was measured with a digital scale to the nearest 0.1 kg, and height was determined by a wall-mounted stadiometer to the nearest 0.5 cm. Body composition was measured by DEXA, using a whole-body scanner. For all patients, right-side half-body scans were carried out from which whole-body composition was extrapolated [48, 49]. MM corresponded to the appendicular LBM (the MM of the arms and legs), and was determined as the difference between total LBM and truncal LBM after removing the contribution of bone.

Serum trace element analysis

Copper and zinc concentrations in serum were measured by fame atomic absorption spectrometry following a one in four dilution with water. Typical between-batch precision for these assays was 3.9 and 2.27%, respectively.

Statistics

All analyses were defined a priori. The results were given as arithmetic mean with SD. ANOVA was used for group comparisons. Adjusted analyses were made using ANCOVA. Baseline associations between continuous variables were analyzed using Pearson correlation coefficients [50-52]. Tests were two-tailed and a p value <0.05 was considered significant. The statistical analysis was performed using Windows 19.0 version of SPSS software (SPSS Inc., Chicago, IL, USA).

Results and discussion

Baseline Data

At baseline, before patients underwent laparoscopic sleeve gastrectomy surgery, there were no statistically significant differences between the group of patients directed for surgical treatment and the control group, regarding age, height, weight, LBM, FM, MM, serum copper or serum zinc concentrations (table 1). None of the patients in this study had any complications during the surgical performance or during the 1-year follow-up period.

Data at 12-months follow-up

Serum zinc concentration decreased in the experimental group, from 77.3 to 63 μg/dL ($p < 0.001$). The same exact trend was observed during the corresponding period in the control group, from 77.1 to 76.6 μg/dL ($p = 0.008$). The intergroup difference in serum zinc concentrations at the 12-months follow-up ($p < 0.001$) was significant (fig. 1).

Serum copper concentrations decreased from 147 μg/dL before laparoscopic sleeve gastrectomy surgery to 90.2 μg/dL at the 1-year follow-up ($p < 0.001$) and increased from 147.1 to 147.6 μg/dL in the control group ($p = 0.021$). The intergroup difference regarding serum magnesium at the 12-months follow-up was statistically significant ($p < 0.001$) (fig. 2).

In the experimental group, the mean LBM decreased

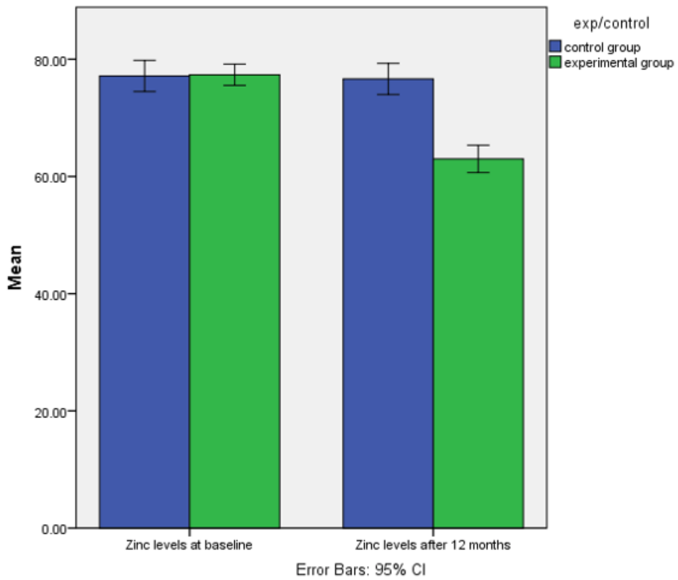

Fig. 1 Changes in serum zinc (μg/dL) from baseline to 1-year follow-up in obese patients treated with laparoscopic sleeve gastrectomy surgery compared to untreated controls

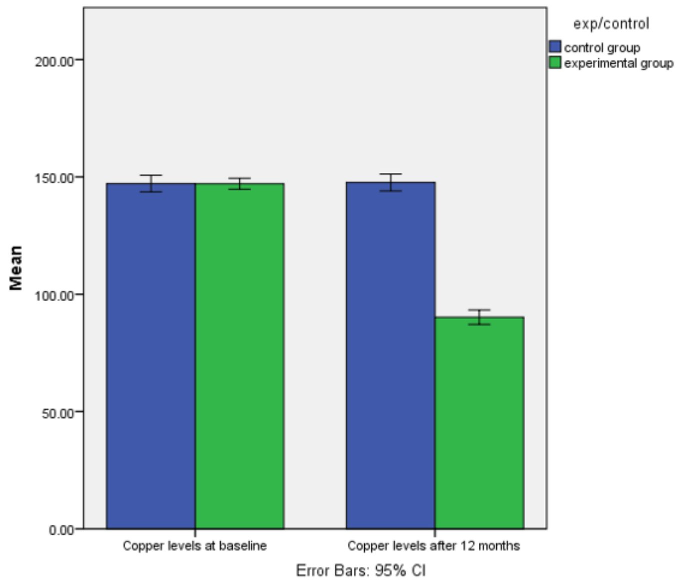

Fig. 2 Changes in serum copper(μg/dL) from baseline to 1-year follow-up in obese patients treated with laparoscopic sleeve gastrectomy surgery compared to untreated controls

from 57.2 kg at baseline to 47.2 kg, ($p < 0.001$). In the control group, a small change but non-significant in mean LBM was observed between baseline and 12 months follow-up, LBM 57.1 kg and 57.2 kg, respectively, $p = 0.095$. LBM was significantly different in the two groups at the 12 months follow-up ($p < 0.001$) (fig. 3).

Regarding the fat mass, in the experimental group, the mean FM decreased from 56.8 kg at baseline to 30.6 kg after 1 year ($p < 0.001$). In the control group, a small change but again non-significant in mean FM was observed between baseline and 1 year follow-up, FM 56.7 kg and 56.8 kg, respectively $p = 0.067$. FM was significantly different in the two groups at the 1 year follow-up ($p < 0.001$) (fig. 4).

When we analyzed the difference between the baseline and after 1 year data regarding the muscle mass, a decrease was observed in the experimental group, from 25.5 to 20.6 kg ($p < 0.001$), while the MM in the control group remained approximately the same during the 12-months period, 25.43 and 25.46 kg ($p = 0.278$). The intergroup difference regarding the MM at the 12-months follow-up ($p = 0.002$) was significant (fig. 5).

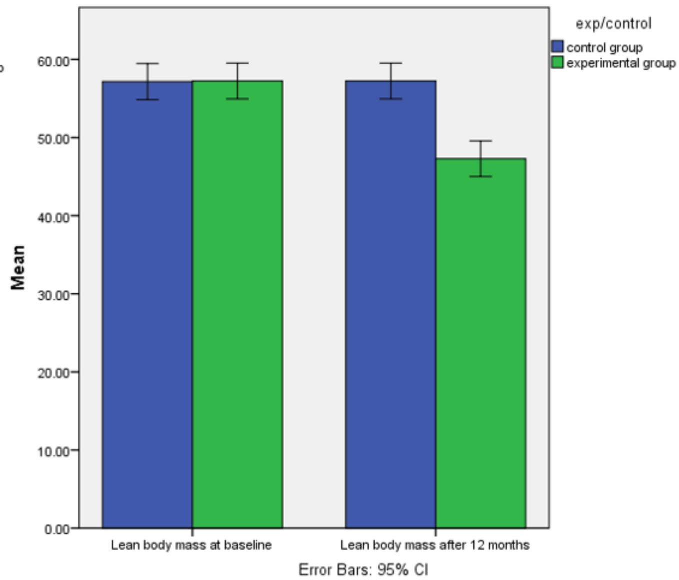

Fig. 3. Changes in lean body mass (kg) from baseline to 1-year follow-up in obese patients treated with laparoscopic sleeve gastrectomy surgery compared to untreated controls.

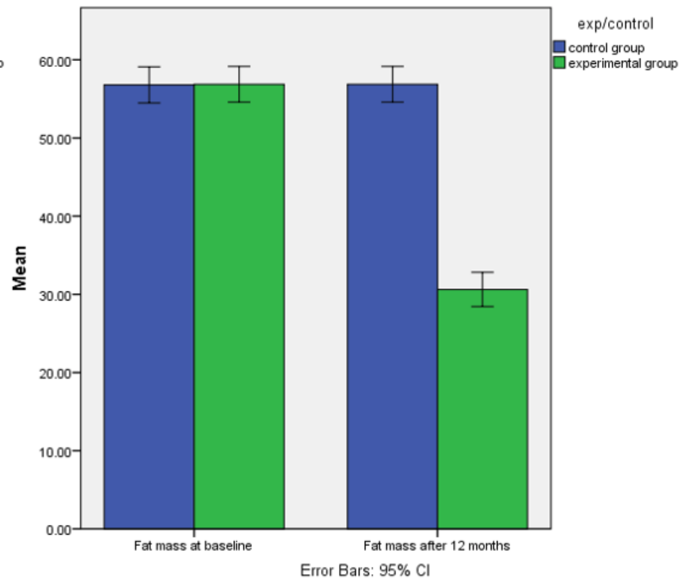

Fig. 4 Changes in fat mass (kg) from baseline to 1-year follow-up in obese patients treated with laparoscopic sleeve gastrectomy surgery compared to untreated controls

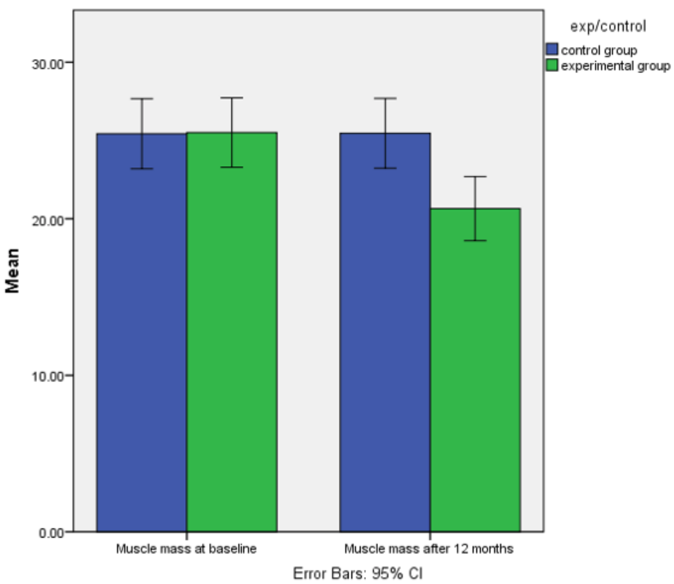

Fig. 5. Changes in muscle mass (kg) from baseline to 1-year follow-up in obese patients treated with laparoscopic sleeve gastrectomy surgery compared to untreated controls

Adjusted analyses - ANCOVA

When we controlled the preoperation values, using ANCOVA, the statistical significance difference between control and experimental groups 12 months post operation maintained for all the measured variables (serum zinc, serum copper, LBM, FM and MM) ($p < 0.001$).

Average LBM taken at baseline was 57.2±10.9 kg, with average ponderal loss of 10.0 kg 12 months after bariatric surgery. These results are in concordance with those found in the literature. For example, in a study by Aquino et al. [53], where 114 patients undergoing bariatric surgery were evaluated and found to have a LBM average of 64.43 kg preoperation to 51.39 kg 6 months post-surgery. The same study found an average drop in FM from 58.41 at baseline to 36.40 after 6 months. Another study on 123 patients, by Hartwig el al. [54], found a drop in LBM from 65.4 kg to 61.0 kg only one month after bariatric surgery. The same study showed a drop in mean FM from 60.1 kg to 50.4 kg. A bariatric surgery is considered to be successful when patients show a ponderal loss over 30% of their preoperative weight. A satisfactory outcome of a bariatric surgery is considered when 25% of their preoperative weight is lost; and unsatisfactory when they lose fewer than 25% of their total weight [55].

Therefore, the patients we studied lost 28.5% of their FM after 12 months after laparoscopic sleeve gastrectomy. Surgery could thus be classified as successful. However, the patients also lost 19.2% of their muscle mass, which may be a reason to raise concerns about future health.

As before mentioned, bariatric surgery's main benefit lies on reducing comorbidities associated with obesity. It is demonstrated that even a slight drop in weight is enough to have a positive effect on type 2 diabetes, hypertension, and dyslipidemia [56, 57]. Furthermore, a 10% drop in weight leads to better long-term control of these same conditions [58].

The significant decrease in MM (from 25.5 kg to 20.6 kg) observed in the experimental group may be explained by the large caloric deficit that is created after the drastic total body weight lost. Large drops in weight are usually followed by a significant drop in basal metabolic rate (BMR), to the tune of hundreds of kilocalories [59]. If we add the hypocaloric diets often prescribed post-surgery that boost proteolysis to meet metabolic demands, we might explain the drop in MM. Furthermore, when this caloric deficit is not followed by sustained physical exercise, which has many benefits including boosting resting metabolic rate and stimulating protein synthesis in the muscles [60, 61], basal metabolic rate was found to drop by 15% to 30% in some studies, making it impossible to maintain a healthy body composition in the long term [62]. However, there is a consensus that obese individuals, regardless of age, have a greater absolute maximum muscle mass and strength compared to non-obese persons, suggesting that increased adiposity acts as a chronic overload stimulus on the antigravity muscles (quadriceps, calf and other muscles), thus increasing muscle size and strength [63]. Therefore, when the overload stimulus is decreased (the body-weight) a drop in muscle mass should be expected.

In addition, protein intake was found to predict the extent of muscle lost after bariatric surgeries. At the end of the first postoperative year, greater protein intake was conducive to the weight lost being primarily in fat. In a study where the authors used stable isotope techniques, on 82 individuals following bariatric surgery, the results showed an 18% drop in lean mass and 82% drop in fat after 4 months [64]. Another study found that 12-months after bariatric surgery, a 20–30% loss in lean mass was found. The amount of fat lost was found to range between 70% and 80% of total weight loss by the patients [65].

The importance of physical activity after bariatric surgery is undeniable, physical exercise can speed up weight loss and preserve LBM. It has been proven that patients who performed physical exercises after bariatric surgery gained 15% LBM, while those who remained sedentary lost 11% LBM by the end of the first year of observation [66]. Therefore, engaging in physical activities is a determining factor in the drop in FM and gains in LBM and MM. Another, study by Herring et al [67], 24 patients who underwent bariatric surgery, recorded a 5.6 kg difference between groups in body mass change from baseline to 24 weeks favoring the exercise group.

In addition, it has been found that body fat percentage and FM are more direct indicators of the gravity of obesity than BMI [68]. Furthermore, it has also been shown that premature death is inversely proportional to gains in FM and reductions in LBM [69, 70]. As before mentioned, a significant drop in LBM results in a drop in basal metabolic rate [71], which is of a higher importance during postoperative care, given how an adequate protein intake and engaging in rigorous physical exercises may moderate, or even outweigh the negative effects of a carbohydrate-restrictive, caloric-deficit diet. That is the reason why regularly physical activities play such an important role in the maintenance or in the improvement of lean muscle mass [72, 73].

However, despite physical activity being an important method for optimizing surgical outcomes after laparoscopic sleeve gastrectomy, it should be taken into consideration that it can sometimes lead to a compensatory response of increased caloric intake [74]. The American Society for Metabolic and Bariatric Surgery has reported that exercise changes body composition, with increased lean body mass resulting in slower loss of overall body mass [74]. The frequency and intensity of exercise may also affect metabolic rate contributing to weight loss plateaus, further studies should asses how different types of exercises, with different frequencies performed at different levels of intensity, influence the total weight lost and the body composition after bariatric surgeries.

In connection to physical activities, there is well known that trace elements like zinc and copper are directly involved as enzymatic co-factors in maintaining and regulating many physiological processes, especially those related to physical exercise [75-77]. In fact, zinc is a structural component of several enzymes, among which are carbonic anhydrase and copper is in the structure of SOD, LDH and cytochrome oxidase. Therefore, it is important to determine whether bariatric surgery alters plasma levels of these metals, as this could be a possible cause of deficit, necessitating a supplementation to maintain enzyme efficiency especially if the patients are regularly engaging in physical activities.

In addition, patients undergoing laparoscopic sleeve gastrectomy are at risk for impaired copper status due to hypo acidity in the remnant stomach pouch and because of bypass of the duodenum. In our study we find a clear trend for change in serum copper levels after bariatric procedures, in the sense of a statistically significant difference between the experimental group and the controls, 90.2 μg/dL compared to 147.6 μg/dL, respectively ($p < 0.001$). In concordance with our results, previous studies have shown that the concentration of blood copper decreases following bariatric surgery [78-80]. Furthermore, there are numerous reports of severe cases of copper deficiency after these surgeries [79-81]. The prevalence of copper deficiency ranges from 10 to 15% in cross-sectional studies and 4 to 18% in longitudinal studies [78-80, 82, 83]. Other than bariatric surgeries, other risk factors for copper deficiency include high zinc supplementation, and insufficient copper in micro nutrient supplementation [78]. Regarding the serum zinc level, in our sample we found a statistically significant difference between the laparoscopic sleeve gastrectomy group and the control group after 12 months, 76.6 μg/dL compared to 63.0, respectively ($p < 0.001$). Before the operation, we did not observe significant deficiencies in any of the trace elements that we measured and it is important to mention that our preoperative sample (experimental group plus control group) was significant ($n = 179$). The mean serum zinc was 77.2 μg/dL and for serum copper 147.0μg/dL. These results at baseline are in contrast to other studies which have demonstrated that obesity is associated with lower circulating concentrations of many micronutrients and greater prevalence of biochemical deficiencies. The mechanisms underlying these observations are likely diverse but, as before mentioned, include effects of inflammation on nutrient transporter proteins as well as greater volumes of distribution given expanded adipose and body water compartments [84]. In addition, obesity and weight gain have been associated with poor food choices, suggesting that despite high caloric intake, micronutrient intake in obese patients is deficient [84-86]. In addition to the inadequate nutrient intake in obesity, it has been showed that nutrient metabolism is also altered in the obese population. Some authors suggest that chronic inflammation associated with obesity may dysregulate nutrient homeostasis, alter synthesis of binding proteins, or even increase oxidative stress, therefore, resulting in an increase usage of antioxidant nutrients [87, 88]. Additionally, although our mean values for both zinc serum and copper serum were significantly lower when compared to the matched control group, the values remained in the normal ranges for both minerals (70-150 μg/dL for copper and 60-144 for zinc). However, it still remains a concern and frequent and thorough evaluations are necessary.

Conclusions

Bariatric surgery has been proven to be an effective tool in achieving absolute weight loss and reducing fat tissue, in morbidly obese population. However, a diet rich in micronutrients and with an adequate protein intake should be prescribed to minimize the loss of lean body mass, and to counteract the post operation mineral deficiencies. In addition, physical exercises, aerobic or strength training should be performed regularly to reduce the negative impact that this operation has on muscle mass and muscle strength.

References

1.BUCHWALD, H., AVIDOR, Y., BRAUNWALD, E., JENSEN, M.D., PORIES, W., FAHRBACH, K., SCHOELLES,, K., Bariatric surgery: a systemic review and meta-analysis. JAMA, **292**, 2004, pp. 1724-1737.

2.ADAMS, T.D., GRESS, R.E., SMITH, S.C., HALVERSON, R.C., SIMPER, S.C., ROSAMOND, W.D., LAMONTE, M.J., STROUP, A.M., HUNT, S.C., Long-term mortality after gastric bypass surgery, N. Engl. J. Med., **357**, 2007, pp. 753–761.

3.SJÖSTRÖM, L., LINDROOS, A.K., PELTONEN, M., TORGERSON, J., BOUCHARD, C., CARLSSON, B., DAHLGREN, S., LARSSON, B., NARBRO, K., SJOSTROM, C.D., SULLIVAN, M., WEDEL, H., Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery, N. Engl. J. Med., **351**, 2004, pp. 2683–2693.

4.BUCHWALD, H., WILLIAMS, S.E., Bariatric surgery worldwide 2003, Obes. Surg., **14**, 2004, pp. 1157–1164.

5.MAGGARD, M.A., SHUGARMAN, L.R., SUTTORP, M., MAGLIONE, M., SUGERMAN, H.J., LIVINGSTON, E.H., NGUYEN, N.T., LI, Z., MOJICA, W.A., HILTON, L., RHODES, S., MORTON, S.C., SHEKELLE, P.G., Meta-analysis: surgical treatment of obesity, Ann. Intern. Med., **142**, 2005, pp. 547–559.

6.TIMOFTE, D., TOARBA, C., HOGAS, S., COVIC, A., CIOBICA, A., CHIRITA, R., LEFTER, R., ARHIRE, L., ARCAN, O., ALEXINSCHI, O., SERBAN, D., GRAUR, M., POROCH, V., The Relevance of Oxidative Stress Status in Type 2 Diabetes and the Chronic Consumption of Alcohol, Rom. Biotech. Lett., **21**, 2016, pp. 11246-11253.

7.TROFIN, F., CIOBICA, A., COJOCARU, D., CHIRAZI, M., HONCERIU, C., TROFIN, L., SERBAN, D., TIMOFTE, D., COJOCARU, S., ANTON, E., Increased oxidative stress in rat after five minutes treadmill exercise, Central European Journal of Med., **9**, 2014, pp 722-728.

8.ANTON, E., ROTARU, A., COVATARIU, D., CIOBICA, A., TIMOFTE, D., POPESCU, R., ANTON, C., Links between extremely high frequency electromagnetic waves and their biological manifestations, Archives of Biological Sci., **67**, 2015, pp. 895-897.

9.TROFIN, F., CIOBICA, A., HONCERIU, C., COJOCARU, S., STOICA, B., COJOCARU, D., CIORNEA, E., TIMOFTE, D., Modulatory effects of vitamin C and smoking status in the relation between physical exercising and oxidative stress, Romanian Biotechnological Lett., **22**, 2017, pp. 12439-12447.

10.PADURARIU, M., PREPELITA, R., CIOBICA, A., DOBRIN, R., TIMOFTE, D., STEFANESCU, C., CHIRITA, R., The concept of suicide: neurophysiological/genetic theories and possible oxytocin relevance, Neurophysiol., **48**, 2016, pp. 312-321.

11.TIMOFTE, D., LIVADARIU, R., BINTINTAN, V., DIACONU, C., IONESCU, L., SANDBERG, A.A., MARICIUC, D.C., DÃNILÃ, R., Metabolic disorders in patients operated for pancreatic cancer. Rev Med Chir Soc Med Nat Iasi., **118**, 2014, pp. 392-398.

12.BALMUS, I., CIOBICA, A., ANTIOCH, I., DOBRIN, R., TIMOFTE, T., Oxidative Stress Implications in the Affective Disorders: Main Biomarkers, Animal Models Relevance, Genetic Perspectives, and Antioxidant Approaches, Oxidative Medicine and Cellular Longev., **1**, 2016, pp. 1-25.

13.ANTIOCH, I., CIOBICA, A., PAULET, M., BILD, V., LEFTER, R., TIMOFTE, D., Pain manifestations in schizophrenia - clinical and experimental aspects in human patients and animal models, Psychiatr. Danub., **27**, 2015, pp. 142-152.

14.CIOBICA, A., PADURARIU, M., CIOBICA, A., TIMOFTE, D., STEFANESCU, C., NASREDDINE, Z., General issues encountered while diagnosing mild cognitive impairment in Romanian patients, International Journal of Geriatric Psychiatr., **32**, 2017, pp.116–117.

15.DRÃGAN, F., LUPU, V.V., PALLAG, A., BARZ, C., FODOR, K., IOP Conference Series: Materials Science and Engineering, **200**, 2017, Paper no. 012063 doi:10.1088/1757-899X/200/1/012063.

16.CHASTON, T.B., DIXON, J.B., O'BRIEN, P.E., Changes in fat-free mass during significant weight loss: a systematic review, Int J Obes (Lond), **31**, 2007, pp. 743–50.

17.CAREY, D.G., PLIEGO, G.J., RAYMOND, R.L., Body composition and metabolic changes following bariatric surgery: effects on fat mass, lean mass and basal metabolic rate: six months to one-year follow-up, Obes Surg., **16**, 2006, pp. 1602–1608.

18.DAS, S.K., ROBERTS, S.B., KEHAYIAS, J.J., WANG, J., HSU, L.K., SHIKORA, S.A., SALTZMAN, E., MCCRORY, M.A., Body composition assessment in extreme obesity and after massive weight loss induced by gastric bypass surgery, Am. J. Physiol. Endocrinol. Metab., **284**, 2003, E1080–1088.

19.CIANGURA, C., BOUILLOT, J.L., LLORET-LINARES, C., POITOU, C., VEYRIE, N., BASDEVANT, A., Dynamics of change in total and regional body composition after gastric bypass in obese patients, Obesity (Silver Spring), **18**, 2010, pp. 760–765.

20.MOIZE, V., ANDREU, A., RODRIGUEZ, L., FLORES, L., IBARZABAL, A., LACY, A., JIMENEZ, A., VIDAL, J., Protein intake and lean tissue mass retention following bariatric surgery, Clin. Nutr., **32**, 2013, pp. 550–555.

21.LEVITT, D.G., BECKMAN, L.M., MAGER, J.R., VALENTINE, B., SIBLEY, S.D., BECKMAN, T.R., KELLOGG, T.A., IKRAMUDDIN, S., EARTHMAN, C.P., Comparison of DXA and water measurements of body fat following gastric bypass surgery and a physiological model of body water, fat, and muscle composition, J Appl Physiol., **109**, 2010, pp. 786–795.
22.WISSE, B.E., KIM, F., SCHWARTZ, M.W., Physiology. An integrative view of obesity, Science, **318**, 2007, pp. 928–929.
23.FOGARTY, A.W., GLANCY, C., JONES, S., LEWIS, S.A., MCKEEVER, T.M., BRITTON, J.R., A prospective study of weight change and systemic inflammation over 9 y., Am J Clin Nutr., **87**, 2008, pp. 30–35.
24.PEPYS, M.B., The acute phase response and C-reactive protein, in: WEATHERALL, D.J., LEDINGHAM, J.G. and WARRELL, D.A., editors. Oxford Textbook of Medicine. Oxford: Oxford University Press; 1996. pp. 1527–1533.
25.CIUBOTARIU, D., GHICIUC, C.M., LUPUSORU, R.V., BIBIRE, N., AGOROAEI, L., LUPUSORU, C.E., Farmacia, **63,** no. 6, 2015, p. 835.
26.NATIONAL ACADEMY OF SCIENCES, Dietary reference intakes for vitamin A vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington, DC: National Academies Press, 2001, pp. 442– 500.
27.LINDER, M.C., GOODE, C.A., Biochemistry of Copper. New York: Plenum Press, 1991, pp. 119.
28.KINSMAN, G.D., HOWARD, A.N., STONE, D.L., MULLINS, P.A., Studies in copper status and atherosclerosis, Biochem Soc Trans., **18**, 1990, pp.1186–1188.
29.MILNE, D.B., Assessment of copper nutritional status, Clin Chem., **40**, 1994, pp. 1479–1484.
30.BERGOMI, M., ROVESTI, S., VINCETI, M., VIVOLI, R., CASELGRANDI, E., VIVOLI, G., Zinc and copper status and blood pressure, J Trace Elem Med Biol., **11**, 1997, pp. 166–169.
31.MIELCARZ, G.W., HOWARD, A.N., WILLIAMS, N.R., KINSMAN, G.D., MORIGUCHI, E., MORIGUCHI, Y., MIZUSHIMA, S., YAMORI, Y., Copper and zinc status as a risk factor for ischemic heart disease: a comparison between Japanese in Brazil and Okinawa, J Trace Elem Exp Med., **10**, 1997, pp. 29–35.
32.JOHNSON, W.T., JOHNSON, L.A., LUKASKI, H.C., Serum superoxide dismutase 3 (extracellular superoxide dismutase) activity is a sensitive indicator of Cu status in rats, J Nutr Biochem., **16**, 2005, pp. 682–692.
33.KLEVAY, L.M., Lack of a recommended dietary allowance for copper may be hazardous to your health. J Am Coll Nutr., **17**, 1998, pp. 322–326.
34.PANG, Y., MACINTOSH, D.L., RYAN, P.B., A longitudinal investigation of aggregate oral intake of copper, J Nutr., **131**, 2001, pp. 2171–2176.
35.KUMAR, N., AHLSKOG, J.E., GROSS, JR. J.B., Acquired hypocupremia after gastric surgery, Clin Gastroenterol Hepatol., **2**, 2004, pp. 1074–1079.
36.KELKAR, P., CHANG, S., MULEY, S.A., Response to oral supplementation in copper deficiency myeloneuropathy, J Clin Neuromuscul Dis., **10**, 2008, pp. 1–3.
37.GRIFFITH, D.P., LIFF, D.A., ZIEGLER, T.R., ESPER, G.J., WINTON, E.F., Acquired copper deficiency: a potentially serious and preventable complication following gastric bypass surgery, Obesity (Silver Spring), **17**, 2009, pp. 827–831.
38.SHAH, M., SIMHA, V., GARG, A., Review: long term impact of bariatric surgery on body weight, comorbidities, and nutritional status, J Clin Endocrinol Metabol., **91**, 2006, pp. 4223–4231.
39.SUGARMAN, H.J., Bariatric surgery for severe obesity, J Assoc Acad Minor Phys., **12**, 2001, pp. 129–136.
40.AGHEORGHIESEI CORODEANU, D.T., POROCH, V., A possible theoretical model of ethical system management in healthcare institutions, 6th LUMEN International Conference on Rethinking Social Action Core Values, 16-19 April 2015, Iasi, Romania, Rethinking Social Action. Core Values, p. 33-41.
41.TOADER, E., TOADER, T., Revista Romana de Bioetica, **10**, no. 3, 2012, p. 66.
42.TOADER, E., Revista Romana de Bioetica, **8**, no. 2, 2010, p. 157.
43.BALAN, G.G., TRIFAN, A., SAVIN, C., BALAN, A., GOLOGAN, E., Revista de Cercetare si Interventie Sociala, **55,** 2016, pp. 244-259.
44.BALAN, G.G., MITRICA, D.E., IACOB, M., BALAN, A., ZETU, I., Revista de Cercetare si Interventie Sociala, **49,** 2015, pp. 229-238.
45.BALAN, A., SAVIN, C., BALAN, G.G., ZETU, I., Revista de Cercetare si Interventie Sociala, **45,** 2014, pp. 160-174.
46.TOADER, E., Revista de Cercetare si Interventie Sociala, **37**, 2012, p. 144.
47.TOADER, E., BALAN, G.G., ILIESCU, D.B., PERJU-DUMBRAVA, D., Romanian Journal of Legal Medicine, **25,** no. 1, 2017, p. 125.
48.TIMOFTE, D., OCHIUZ, L., URSARU. M., CIUNTU, B., IONESCU, L., CALU, V., MOCANU, V., PUIA, I.C., Rev. Chim. (Bucharest), **68**, no. 10, 2017, pp. 2341- 2345.
49.TIMOFTE, D., OCHIUZ, L., URSARU. M., CIUNTU, B., HRISTOV, I., PUIA, I.C., CALU, V., MOCANU, V., Rev. Chim. (Bucharest), **68**, no. 9, 2017, pp. 1997-2001.
50.DOBRIN, R., CIOBICA, A., TOADER, E., POROCH, V., Rev. Chim. (Bucharest), **67**, no. 9, 2016, p. 1778.
51.ALEXA, A.I., CANTEMIR, A., CIOBICA, A., GARDIKIOTIS, I., ANTIOCH, I., HONCERIU, C., ZAMFIR, C.L., POROCH, V., Rev. Chim. (Bucharest), **68**, no. 1, 2017, p. 90-93.
52.CANTEMIR, A., ALEXA, A.I., CIOBICA, A., TOADER, E., BALMUS, I.M., COJOCARU, S.I., CHISELITA, D., COSTIN, D., Rev.Chim. (Bucharest), **67**, no. 9, 2016, pp. 1725-1727.
53.DE AQUINO, L.A., PEREIRA, S.E., DE SOUZA SILVA, J., SOBRINHO, C.J., RAMALHO, A., Bariatric surgery: impact on body composition after Roux-en-Y gastric bypass, Obes Surg., **22**, 2012, pp. 195-200.
54.HARTWIG T.W., INSAURRIAGA DOS SANTOS, F.A., GONZALEZ, M.C., ROMBALDI, A.J., Effects of bariatric surgery on the body composition of adults, Rev. bras. cineantropom. desempenho hum., **15**, 2013, pp. 686-694.
55.MACLEAN, L.D., RHODE, B.M., SHIZGAL, H.M., Gastroplasty for obesity, Surg Gynecol Obstet., **153**, 1981, pp. 200–208.
56.BUSETTO, L., PISENT, C., RINALDI, D., LONGHIN, P.L., SEGATO, G., DE MARCHI, F., FOLETTO, M., FAVRETTI, F., LISE, M., ENZI, G., Variation in lipid levels in morbidly obese patients operated with the Lap-Band® adjustable gastric banding system: effects of different levels of weight loss, Obes Surg., **10**, 2000, pp. 569–577.
57.INGE, T.H., XANTHAKOS, S.A., ZELLER, M.H., Bariatric surgery for pediatric extreme obesity: now or later?, Int J Obese (Lond)., **31**, 2007, pp. 1–14.
58.KUHLMANN, H.W., FALCONI, R.A., WOLF, A.M., Cost-effective bariatric surgery in Germany today, Obes Surg., **10**, 2000, pp. 549–552.
59.HILL, J.O., SPARLING, P.B., SHIELDS, T.W., HELLER, P.A., Effects of exercise and food restriction and body composition and metabolic rate in obese women, Am J Clin Nutr., **46**, 1987, pp. 622–630.
60.STIEGLER, P., CUNLIFFE, A., The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss, Sports Med., **36**, 2006, pp. 239–262.
61.CIOLAC, E.G., GUIMARÃES, G.V., Exercício físico e síndrome metabolica, Rev Bras Med Esporte, 10, 2004, pp. 319–324.
62.RAVUSSIN, E., LILLIOJA, S., KNOWLER, W., CHRISTIN, L., FREYMOND, D., ABBOTT, W.G, BOYCE, V., HOWARD, B.V., BOGARDUS, C., Reduced rate of energy expenditure as a risk factor for body-weight gain, N Engl J Med., **318**, 1988, pp. 467–472.
63.TOMLINSON, D.J., ERSKINE, R.M., MORSE, C.I., WINWOOD, K., ONAMBELE-PEARSON, G., The impact of obesity on skeletal muscle strength and structure through adolescence to old age, Biogeront., **17**, 2016, pp. 467–483.
64.PALOMBO JD, MALETSKOS CJ, REINHOLD RV, HAYWARD, E., WADE, J., BOTHE, A., BENOTTI, P., BISTRIAN, B.R., BLACKBURN, G.L., Composition of weight loss in morbidly obese patients after gastric bypass, J Surg Res., **30**, 1981, pp. 435–442.
65.VAN GEMERT, W.G., WESTERTERP, K.R., VAN ACKER, B.A., Energy, substrate and protein metabolism in morbid obesity before, during and after massive weight loss, Int J Obes Relat Metab Disord., **24**, 2000, pp. 711–718.

66.METCALF, B., RABKIN, R.A., RABKIN, J.M., METCALF, L.J., LEHMAN-BECKER, L.B., Weight loss composition: the effects of exercise following obesity surgery as measured by bioelectrical impedance analysis, Obes Surg., **15**, 2005, pp. 183–186.
67.HERRING, L.Y., STEVINSON, C., CARTER, P., BIDDLE, S.J., BOWREY, D., SUTTON, C., DAVIES, M.J., The effects of supervised exercise training 12-24 months after bariatric surgery on physical function and body composition: a randomised controlled trial, Int J Obes (Lond)., **41**, 2017, pp. 909-916.
68.NAGAYA, T., YOSHIDA, H., TAKAHASHI, H., MATSUDA, Y., KAWAI, M., Body mass index (weight/height2) or percentage body fat by bioelectrical impedance analysis: which variable better reflects serum lipid profile?, Int J Obes., **23**, 1999, pp. 771–774.
69.JACKSON, A.S., STANFORTH, P.R., GAGNON, J., RANKINEN, T., LEON, A.S., RAO, D.C., SKINNER, J.S., BOUCHARD, C., WILMORE, J.H., The effect of sex, age and race on estimating percentage body fat from body mass index: the heritage family study, Int J Obes., **26**, 2002, pp. 789-796.
70.RESIDORI, L., GARCIA-LORDA, P., FLANCBAUM, L., PI-SUNYER, F.X., LAFERRERE, B., Prevalence of comorbidities in obese patients before bariatric surgery: effect of race, Obes Surg., **13**, 2003, pp. 333–340.
71.KARHUNEN, L., FRANSSILA-KALLUNKI, A., RISSANEN, A., KERVINEN, K., KESÄNIEMI, Y.A., UUSITUPA, M., Determinants of resting energy expenditure in obese nondiabetic Caucasian women, Int J Obes. Lond., **21**, 1997, pp. 197– 202.
72.LIOU, Y.M., LIOU, T.H., CHANG, L.C., Obesity among adolescents: sedentary leisure time and sleeping as determinants, Journal of Advanced Nursing., **66**, 2010, pp. 1246–1256.
73.STIEGLER, P., CUNLIFFE, A., The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss, Sports Med., **36**, 2006, pp. 239–262.
74.*** American Society of Metabolic and Bariatric Surgery, ASMBS Public and Professional Education Committee Bariatric Surgery: Postoperative Concerns, 2008.
75.ANDERSON, R.A., POLANSKY, M.M., BRYDEN, N.A., Acute effects on chromium, copper, zinc, and selected clinical variables in urine and serum of male runners, Biol Trace Elem Res., 6, 1984, pp. 327-336.
76.OHNO, H., YAMASHITA, K., DOI, R., YAMAMURA, K., KONDO, T., TANIGUCHI, N., Exercise-induced changes in blood zinc and related proteins in humans. J Appl Physiol., 58, 1985, pp. 1453-1458.
77.OLHA, A.E., KLISSOURAS, V., SULLIVAN, J.D., SKORYNA, S.C., Effect of exercise on concentration of elements in the serum, J. Sports. Med. Phys. Fitness., 22, 1982, pp. 414–425.
78.ROJAS, P., CARRASCO, F., CODOCEO, J., INOSTROZA, J., BASFI-FER, K., PAPAPIETRO, K., Traceelement status and inflammation parameters after 6 months of Roux-en-Ygastric bypass, Obes Surg., **21**, 2011, pp. 561–568.
79.GLETSU-MILLER, N., WRIGHT, B.N., Mineral malnutrition following bariatric surgery, Adv Nutr., **4**, 2013, pp. 506–517.
80.GLETSU-MILLER, N., BRODERIUS, M., FREDIANI, J.K., ZHAO, V.M., GRIFFITH, D.P., DAVIS, JR, S.S., Incidence and prevalence of copper deficiency following Roux-en-Y gastricbypass surgery, Int J Obes (Lond)., **36**, 2012, pp. 328–335.
81.O'DONNELL, K.B., SIMMONS, M., Early-onset copper deficiency following Roux-en-Ygastric bypass, Nutr Clin Pract., **26**, 2011, pp. 66–69.
82.GRIFFITH, D.P., LIFF, D.A., ZIEGLER, T.R., ESPER, G.J., WINTON, E.F., Acquired copper deficiency: a potential serious and preventable complication following gastricbypass surgery, Obesity (Silver Spring), **17**, 2009, pp. 827–831.
83.ERNST, B., THURNHEER, M., SCHULTES, B., Copper deficiency after gastric bypass surgery, Obesity (Silver Spring), **17**, 2009, pp. 1980–1981.
84.SALTZMAN, E., KARL, J.P., Nutrient deficiencies after gastric bypass surgery, Annu Rev. Nutr., **33**, 2013, pp. 183–203.
85.FUNG, T.T., RIMM, E.B., SPIEGELMAN, D., RIFAI, N., TOFLER, G.H., WILLETT, W.C., HU, F.B., Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk, Am. J. Clin. Nutr., **73**, 2001, pp. 61–67.
86.LEDIKWE, J.H., SMICIKLAS-WRIGHT, H., MITCHELL, D.C., MILLER, C.K., JENSEN, G.L., Dietary patterns of rural older adults are associated with weight and nutritional status, J Am. Geriat.r Soc., **52**, 2004, pp. 589–595.
87.AASHEIM, E.T., BOHMER, T., Low preoperative vitamin levels in morbidly obesepatients: a role of systemic inflammation?, Surg. Obes. Relat. Dis., **4**, 2008, pp. 779–780.
88.CALDER PC, AHLUWALIA N, BROUNS F, BUETLER T, CLEMENT K, CUNNINGHAM K, ESPOSITO K, JÖNSSON LS, KOLB H, LANSINK M, MARCOS A, MARGIORIS A, MATUSHESKI N, NORDMANN H, O'BRIEN J, PUGLIESE G, RIZKALLA S, SCHALKWIJK C, TUOMILEHTO J, WARNBERG J, WATZL B, WINKLHOFER-ROOB BM., Dietary factors and low-grade inflammation in relation to overweight and obesity, Br. J. Nutr., **106**, 2011, S5–78

Manuscript received: 2.05.2017