Comparative Study between Effects of Omega 3 Fatty Acid Supplements versus Low Caloric Diet in Reducing the Liver Volume in Bariatric Patients Preoperatively, a Randomized Controlled Study

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Background: Bariatric surgery is the most effective treatment for obesity. Its effects go beyond weight loss in a high percentage of cases achieving remission of comorbidities associated with obesity and reducing mortality.

An essential step in laparoscopic bariatric surgery is elevation of the left liver lobe to expose the gastro-esophageal junction. An enlarged and fatty liver complicates the surgical procedure and increases the risk for laceration of the liver. Liver span can be reduced before the operation by very low caloric diet or by Omega 3 capsules.

Patients and methods: This is a prospective randomized study which included 40 morbidly obese patients, divided into two groups; group A those on pre-operative very low caloric diet (VLCD), and group B those on preoperative Omega 3 capsules.

All patients underwent a bariatric procedure in Kasr Alainy Teaching Hospital from August 2019 to February 2020. Preoperative and postoperative evaluation followed the same standard protocol .All patients in both groups underwent pelvi-abdominal ultrasound before and after VLCD and Omega 3 capsules preoperative by the same operator.

Results: In the current study there is statistically significant decrease in the preoperative Liver Span group A (Mean decrease from 13.5±1.6 to 11.9±1.4) and in group B (Mean decrease from 14.4±2.2 to 12.8±2.3) (p value < 0.001). However, no significant difference was found between the two groups.

Conclusion: The low caloric diet outperformed the omega-3 in total liver volume reduction, but the difference was not significant.

Key words: Obesity, bariatric surgery, Liver span, Diet, Omega 3 capsules.

Introduction

Obesity is the second leading cause of preventable death in the United States, currently outdone only by smoking. However, obesity as a separate disease entity is still underappreciated and certainly misunderstood. The fact that the American Medical Association waited until the summer of 2013 to acknowledge obesity as a disease entity illustrates this statement: "Obesity is a disease and is likely multifactorial in its origin".[1]

The degrees of obesity are defined by body mass index (BMI = weight [kg]/height [m2]), which correlates body weight with height. Controversy exists as to the most accurate system by which to classify obesity. BMI has its inaccuracies, especially for the heavily muscled individual who may weigh more but have a low amount of body fat. However, BMI is the clinically easiest system to use, employing the simply measured parameters of height and weight. The World Health Organization classification of obesity is given in **(Table 1)**.[2]

Bariatric operations produce weight loss through at least two mechanisms and probably many more that are not known. The most common is restriction of intake. Malabsorption of ingested food is the second mechanism. Restrictive operations may include no or only a modest malabsorptive component. Malabsorptive operations may have some restrictive component.[3]

Types of commonly performed bariatric operations by mechanism of action:[3]

Primarily restrictive

1. Laparoscopic adjustable gastric banding (LAGB).
2. Sleeve gastrectomy (SG).

Primarily malabsorptive

1. Biliopancreatic diversion (BPD).
2. Duodenal switch (DS).

Combination

1. Roux-en-Y gastricbypass (RYGB).

2. One Anastomosis Gastric Bypass (OAGB)

Indications for bariatric surgery:[3]

Patient must have:

1. Body mass index ≥40 kg/m^2 with or without co-morbid medical conditions associated with obesity.
2. Body mass index 35–40 kg/m2 with co-morbid medical conditions.

In addition, it is expected that the patient

Has failed attempt at medically supervised diet.

Be psychiatrically stable.

Potential contraindications for bariatric surgery:[3]

1. Severe medical disease making anesthesia or surgery prohibitively risky (American Society of Anesthesiologists class IV).
2. Mentally incompetent to understand procedure.
3. Inability or unwillingness to change lifestyle postoperatively.
4. Drug, alcohol, or other addiction.
5. Active problem of bulimia or other eating disorder.
6. Psychologically unstable.
7. Nonambulatory status.
8. Unsupportive home environment

Complications

Although laparoscopic bariatric surgeries are generally regarded as safe , the large number of operations performed each year means that many individuals will suffer a complication during surgery , in the early post-operative phase (Within 30 days after surgery), or at a later stage.

The benefits of surgery must always be interpreted in the context of complications suffered.

Complication rates must be low in order to motivate the use of surgery for treatment of morbid obesity.[4,5]

Most common being

- Bowel injury
- Instrument failure
- Anaesthesia event
- Revision of anastomosis
- Injury to the liver or spleen
- Major vascular injury

So, injury to the liver and specifically the left lobe is one of the intraoperative adverse events that happen during surgery due to enlarged fatty liver and this event can be prevented by shrinking the size of the liver by either two weeks of preoperative diet or four weeks of preoperative omega 3 supplements.[4,5]

Assessment of liver span by ultrasound

A reliable and practical set of three simple measurement planes of the liver using 2D ultrasound: A maximum cranio-caudal length of the liver in the mid-clavicular line (Liver Span), a dome to tip measurement of the liver in the mid-clavicular line and a ventrodorsal (Anterior to posterior) measurement of the liver in the midline.[6]

Preoperative diet for weight loss surgery

In the 2-4 weeks leading up to bariatric surgery, surgeons tend to place their patients on a very-low calorie diet (VLCD).[7] VLCD aims to provide patients with low energy intake, whilst also maintaining a high protein formula, the combination of which results in rapid weight loss, adequate satiety for a few days, and minimizes loss of fat-free mass.[8,9] VLCD has been clinically proven to induce weight loss.[10] With the intention of optimizing safety of the procedure, pre-operative weight loss is ideal. The primary reason for this is that it reduces liver volume, provides greater surgical access, and reduces peri-operative complications.[11,12] The role of VLCD in having these effects can be appreciated when considering the fact that excessive intrahepatic deposition of fat has complicated the technical aspects of surgery and increase operating time.[13,14] Furthermore, an enlarged liver has been reported to be the most common cause for conversion to an open procedure during laparoscopic gastric bypass and gastric banding.[15,16]

It is significant to note that while some VLCD programs may extend for over 12 weeks, research has demonstrated that 80% of the decrease in liver volume in response to VLCD is achieved after the initial 2 weeks.[17] Furthermore, there is concern that an aggressive or prolonged form of this diet may be associated with adverse outcomes such as impaired immunity and poor wound healing.[18] For this reason, in order to reach a balance between maximizing weight loss, and minimizing complications, the preference is to adhere to only 2 weeks of VLCD.[18]

This evidence strongly suggests that in the pre-operative setting, the patient should be commenced on a 2 week very-low calorie diet pre-operatively and to then be fasted from the day of the procedure.[17]

VLCD has to be from 800 to 1000 kcl per day, as well as the recommended daily allowance of essential vitamins, minerals, and trace elements.[11]

Effect of Omega 3 on liver volume

Nonalcoholic fatty liver disease (NAFLD) involves the excess accumulation of hepatic fat in the absence of alcohol consumption and is defined by the presence of steatosis (characterized by lipid droplets) in more than 5% of hepatocytes.[19] The histological pattern of NAFLD can progress to nonalcoholic steatohepatitis (NASH). NAFLD is now one of the most common liver diseases worldwide. In Western countries and some regions of China, the prevalence of NASH and NAFLD is 1–5% and 15–39%, respectively.[20] One-third of NASH patients have advanced fibrosis and 20% develop cirrhosis.[21] The pathogenesis of NAFLD is multifactorial and includes excessive inappropriate dietary fat intake combined with peripheral insulin resistance, oxidative stress, and innate immunity.[22] It is frequently associated with obesity, type 2 diabetes (T2DM), dyslipidemia, metabolic syndrome, and cardiovascular disease.[23-27]

NAFLD is considered to be associated with an excess of n-6 and a deficiency of n-3 polyunsaturated fatty acids (PUFAs) in the diet.[28] Studies have indicated a lower PUFA content and a higher omega-6/omega-3 ratio in NAFLD patients.[29,30] omega-3 PUFAs are negative regulators of hepatic lipogenesis.[31,32] and have a beneficial impact on hypertension, hyperlipidemia, endothelial dysfunction, and cardiovascular disease.[33]

Patients and methods

This is a prospective randomized study which included 40 morbidly obese patients randomly allocated from bariatric clinic in Kasr Alainy Teaching Hospital, divided into two equal groups; group A those on pre-operative very low caloric diet (VLCD) starting 2 weeks before the surgery, and group B those on Omega 3 capsules 3 gm / day for 4 weeks before the surgery.

All patients underwent a bariatric procedure in Kasr Alainy Teaching Hospital during the period from August 2019 to February 2020. Preoperative and postoperative evaluation followed the same standard protocol and included a thorough personal, medical and surgical history, complete specific labs, complete endocrinal workup, psychological testing, and counseling by a dietician .

All patients in both groups underwent pelvi-abdominal ultrasound before and after VLCD and Omega 3 capsules preoperative by the same operator.

Inclusion criteria

The subjects were considered appropriate candidates for the present study

If they were:

1. All morbidly obese patient with BMI more than or equal to 40 kg/m^2 or BMI more than or equal to 35 kg / m^2 with comorbidities.
2. Willing to give consent and comply with the evaluation and treatment schedule, were 18–65 years old.
3. Patients of both genders (Male and female).
4. All appropriate non-surgical measures have been tried but have failed to achieve or maintain adequate, clinically beneficial weight loss for at least six months.
5. Patients are receiving or will receive management in a specialist obesity service.
6. Patients are generally fit for anesthesia and surgery.
7. Patients commit to the need for long-term follow up.
8. Patients needed to demonstrate the Absence of significant psychopathology limiting ability to understand the procedure and comply with the medical, surgical, and/or behavioral recommendations.

Exclusion criteria

1. All patients with risk factors for Omega 3 capsules as liver insufficiency.
2. Any condition that would preclude compliance with the study.

Preoperative preparation

Patients were informed about the nature of the research, and each patient understood and agreed to the procedure. All patients underwent a standard evaluation preoperatively.

Blood tests were requested in the form of:

1. Complete blood picture, Fasting blood sugar.
2. Clinical chemistries (Serum albumin, ALT, AST, Urea, Creatinine). Prothrombin time and concentration.
3. Chest X-ray, and Upper endoscopy were performed preoperatively.
4. Pelvi-abdominal ultrasound 2 times one before (VLCD or Omega 3) and the other after 2 weeks in case of VLCD and 4 weeks in case of Omega 3 capsules in KasrAlainy Radiology Department using Philips iU machine and linear (L9-3), convex (C5-1) and sector (S5-1)probes to detect liver span (% of change).

Post-operative diet regimen

Patients were encouraged of early mobility few hours postoperative. We started administration of

IV proton pump inhibitors (PPIs) from the first day post-operatively, and continued orally after patients started oral feeding for 6-8 weeks.

Patients started oral fluid intake on the first post-operative day.

Gradually diet changed from fluid to solid during 6 to 8 weeks.

All patients were advised to have oral fluids for the first 15 days followed by soft diet until the first postoperative month, and then gradually proceed to regular food with exception of high sugar and fatty foods.

Primary outcome

Liver span by Ultrasound (2 times one before (VLCD or Omega 3) and the other after 2 weeks in case of VLCD and 4 weeks in case of Omega 3 capsules) to detect % of change.

Statistical methods

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25. Data was summarized using mean, Standard deviation, median, minimum and maximum in quantitative data and using Frequency (Count) and relative frequency (Percentage) for categorical data. For Comparison of serial measurements within each patient the non-parametric Wilcoxon signed rank test was used. Correlations between quantitative Variables were done using Spearman correlation coefficient .P-values less than0.05 were considered as statistically significant.

Results

This is a prospective randomized study which included 40 morbidly obese patients randomly allocated , divided into two equal groups ; group A who received pre-operative very low caloric diet (VLCD) 2 weeks before the operation , and group B who received Omega 3 capsules (3 gm / day) for 4 weeks before the operation . All patients underwent a bariatric procedure in KasrAlainy Teaching Hospital during the period from August 2019 to February 2020.

Demographic data

Age distribution:

Mean of Age in group A was 33.2 while in group B was 37. **(Table 2, Figures 1).**

Body Mass Index distribution

BMI in group A ranged from (47-61) with a mean of 54 while in group B ranged from (47-60) with a mean of 54. **(Table 3).**

Methods of treatment

1. Diet Group A (Liver Span pre and post treatment):

   Mean of Liver Span in group A changed from 13.5 before to 11.9 after diet **(Table 4).**

2. Omega 3 Group B (Liver Span pre and post treatment):

   Mean of Liver Span in group B changed from 14.4 before to 12.8 after Omega 3 capsules. **(Table 5).**

Liver span pretreatment

Liver span before treatment in group A ranged from (12-15) with a mean of 13.5 while in group B ranged from (13.4-16) with a mean of 14.4. **(Table 6, Figure 2).**

Liver span post treatment

Liver span after treatment in group A ranged from (11-12) with a mean of 11.9 while in group B ranged from (12.5-14) with a mean of 12.8, with a statistical difference between both groups. **(Table 7, Figure 3)**. However, this difference is likely owing to the preexisting difference found in pre-operative liver span. Thus on comparing percentage of liver span change post ttt, there was no significant difference between both groups. (Pvalue= 0.76) **(Figures 4-8).**

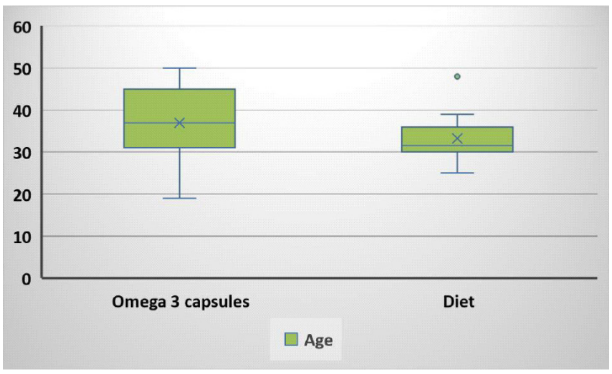

Fig 1: Chart showing age distribution among both groups.

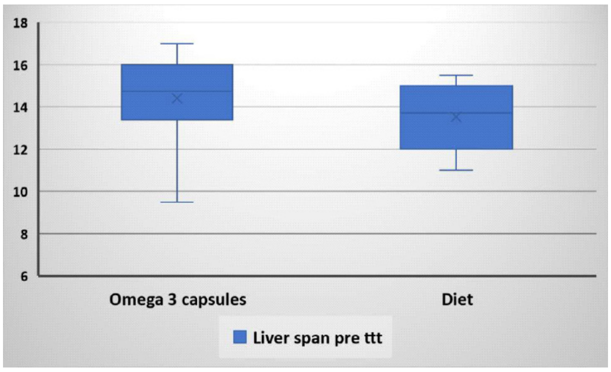

Fig 2: Chart showing difference in liver span pre ttt between both groups.

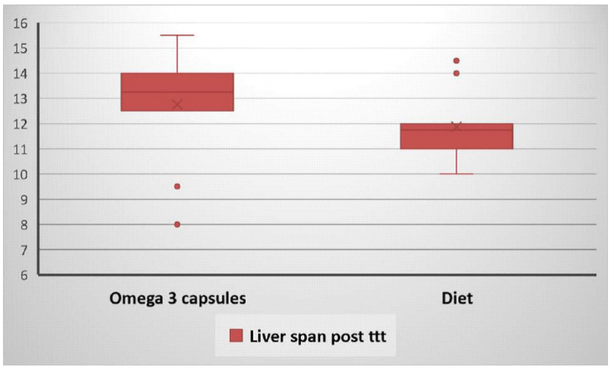

Fig 3: Chart showing difference in liver span post ttt among both groups.

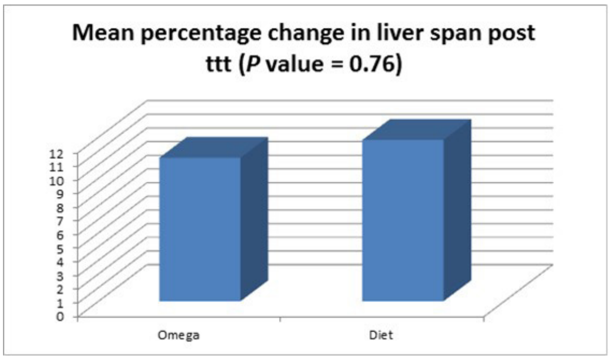

Fig 4: Chart showing mean percentage change in liver span post ttt.

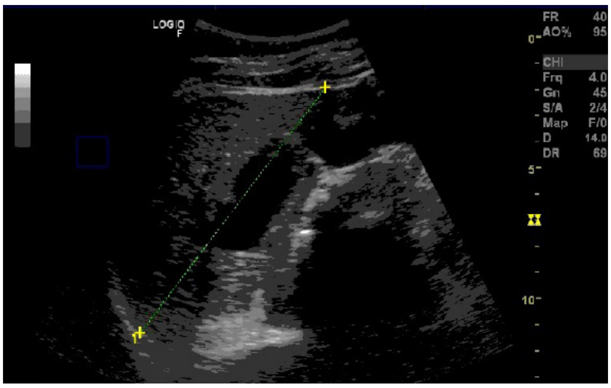

Fig 5: Liver span pre ttt 11.7 cm.

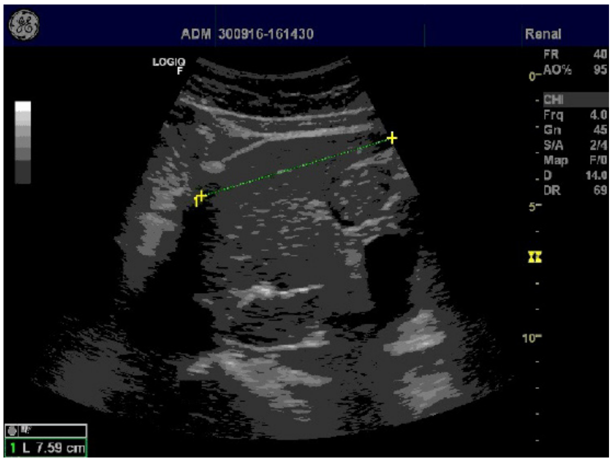

Fig 6: Liver span post ttt 7.59 cm.

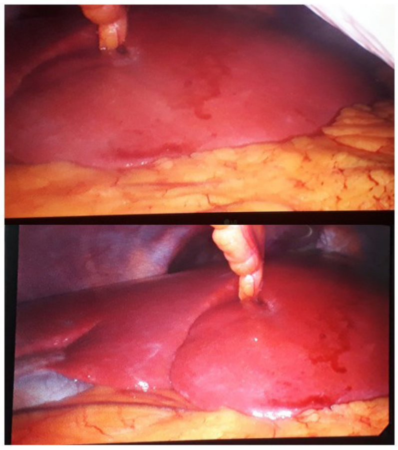

Fig 7: Enlarged fatty liver is aproplem during surgery.

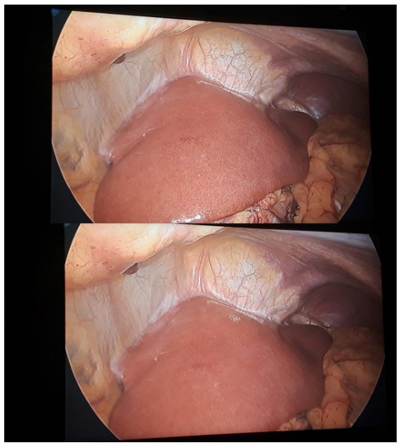

Fig 8: Small sized left lobe after diet or omega 3 supplements.

Table 1: World Health Organization classification of obesity by body mass index BMI (kg/m2)[2]

Normal range	18.5–24.9
Pre-obese	25.0–29.9
Obese class I	30.0–34.9
Obese class II	35.0–39.9
Obese class III	≥40.0

Table 2: Describes age distribution in group A and B

	Diet	**Omega 3 capsules**	**P value**
Mean ± SD	33.2±6.6	37±8.9	0.068
Median (IQR)	31.5(30:36)	37(31:45)	

Table 3: Describes BMI distribution in group A and B

	Diet	**Omega 3 capsules**	**P value**
Mean ± SD	54±8.4	54±8.8	1
Median (IQR)	52(47:61)	52(47:60)	

Table 4: Describes liver span in group A (pre and post ttt)

	Diet		**P value**
Liver Span	Pre	post	
Mean ± SD	13.5±1.6	11.9±1.4	<0.001 S
Median (IQR)	13.7(12:15)	11.8 (11:12)	

Table 5: Describes liver span in group B (Pre and post ttt)

	Omega 3		**P value**
Liver Span	Pre	post	
Mean ± SD	14.4±2.2	12.8±2.3	<0.001 S
Median (IQR)	14.8(13.4:16	13.3(12.5:14)	

Table 6: Describes liver span pre ttt in group A and B

Liver Span pre ttt	**Diet**	**Omega 3 capsules**	**P value**
Mean ± SD	13.5±1.6	14.4±2.2	*0.046 S
Median (IQR)	13.7(12:15)	14.8(13.4:16)	

Table 7: Describes liver span post ttt in group A and B

Liver Span post ttt	**Diet**	**Omega 3 capsules**	**P value**
Mean ± SD	11.9±1.4	12.8±2.3	0.040 S
Median (IQR)	11.8(11:12)	13.3 (12.5:14)	

Discussion

Bariatric surgery is the most effective treatment for patients with severe obesity (Body mass index of greater than or equal 40 kg/m^2), both in terms of weight loss and improvements in obesity-related diseases.[34,35]

In keeping with these marked health benefits, the number of patients undergoing bariatric surgery has reached unprecedented levels, with over 340,000 bariatric procedures undertaken in 2011.[36]

Non-alcoholic fatty liver disease (NAFLD) is a very common condition among obese patients that may lead to the enlargement of the liver that in turn impairs the access to the gastro-esophageal junction during laparoscopic bariatric surgery.[37]

An essential step in laparoscopic bariatric surgery is elevation of the left liver lobe to expose the gastroesophageal junction. An enlarged and fatty liver complicates the surgical procedure and increases the risk for laceration of the liver.[38]

The aim of our study was to evaluate methods to reduce liver volume in patients prior to laparoscopic bariatric surgery. In the current study, 40 morbidly obese patients, those patients were divided into two equal groups; group A on pre-operative very low caloric diet (VLCD) starting 2 weeks before the surgery, and group B on Omega 3 capsules 3 gm / day for 4 weeks before the surgery.

In the current study, we found a statistically significant decrease in the preoperative Liver Span in patients of group A (Mean decrease from 13.5±1.6 to 11.9±1.4) and in patients of group B (Mean decrease from 14.4±2.2 to 12.8±2.3) (p value < 0.001). However, when comparing both groups no significant difference in liver span change post ttt was noted. (P value 0.76).

Conclusion and summary

- Non-alcoholic fatty liver disease (NAFLD) is a very common condition among obese patients that may lead to the enlargement of the liver.
- An enlarged and fatty liver complicates the surgical procedure and increases the risk for laceration of the liver.
- An essential step in laparoscopic bariatric surgery is elevation of the left liver lobe to expose the gastroesophageal junction.
- The Low Caloric Diet and the omega-3 both achieved Left Liver Lobe and Total Liver Volume reduction with no significant difference between them
- Omega-3 fatty acids may provide a safe and more patient-friendly alternative for a Low Caloric Diet to reduce liver volume and left liver lobe span.

References

1. Philip R. Schauer, Bruce Schirmer(ed): The surgical management of obesity. Schwartz's principles of surgery tenth edition. 2015; 1099 – 1105. ***McGrow- HillEducation.***
2. The World Health Organization (WHO) 2000. classifications of obesity by BMI.
3. National Institutes of Health Consensus Conference. Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. ***Ann Intern Med***. 1991; 115: 956-961.
4. Greenstein AJ, Wahed AS, Adeniji A, et al: Prevalence of adverse intraoperative events during obesity surgery and their sequelae. ***J Am CollSurg.*** 2012; 215(2): 271-277 e273.
5. Sundbom M, Ottosson J: Trocar injuries in 17,466 laparoscopic gastric bybass-a nationwide survey from the scandinavian obesity surgery registry. ***Obes Surg***. e-publ 2016.
6. Childs JT, Esterman AJ, Thoirs KA: The development of a practical and uncomplicated predictive equation to determine liver volume from simple linear ultrasound measurements of the liver. ***Radiography.*** 2016; 1;22(2):e125-30.
7. Nielsen LV, Nielsen MS, Schmidt JB, et al: Efficacy of a liquid low-energy formula diet in achieving preoperative target weight loss before bariatric surgery. ***J Nutr Sci.*** 2016; 5.
8. Harder HB, Astrup D: The effect of a rapid weight loss on lipid profile and glycemic control in obese type 2 diabetic patients. ***Int J Obes Relat Metab Disord.*** 2004; 28: 180-182.
9. Piatti PM, Monti F, Fermo I, et al: Hypocaloric high-protein diet improves glucose oxidation and spares lean body mass: Comparison to hypocaloric high-carbohydrate diet. ***Metabolism*** 1994; 43: 1481-1487.
10. Faria SL, Faria OP, de Almeida Cardeal M, et al: Effects of a very low calorie diet in the preoperative stage of bariatric surgery: A randomized trial. ***Surg Obes Relat Dis.*** 2015; 11: 230-237.
11. Van Nieuwenhove Y, Dambrauskas Z, Campillo-Soto A, et al: Preoperative very low-calorie diet and operative outcome after laparoscopic gastric bypass: A randomized multicenter study. ***Arch Surg.*** 2011; 146: 1300-1305.
12. Edholm D, Kullberg J, Haenni A, et al: Preoperative 4-week low-calorie diet reduces liver volume and intrahepatic fat, and facilitates

laparoscopic gastric bypass in morbidly obese. *Obes Surg.* 2011; 21: 345-350.

13. Dixon JB, Bhathal PS, O'Brien PE: Nonalcoholic fatty liver disease: Predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. *Gastroenterology.* 2001; 121: 91-100.

14. McCullough AJ: The clinical features, diagnosis and natural history of nonalcoholic fatty liver disease. *Clin Liver Dis*. 2004; 8: 521-533.

15. Schwartz ML, Drew RL, Chazin-Caldie M: Laparoscopic Roux-en-Y gastric bypass: Preoperative determinants of prolonged operative times, conversion to open gastric bypasses, and postoperative complications. *Obes Surg.* 2003; 13: 734-738.

16. O'Brien PE, Dixon JB, Brown W, et al: The laparoscopic adjustable gastric band (Lap-Band): A prospective study of medium-term effects on weight, health and quality of life. *Obes Surg.* 2002; 12: 652-660.

17. Colles SL, Dixon JB, Marks P et al: Preoperative weight loss with a very-low-energy diet: Quantitation of changes in liver and abdominal fat by serial imaging. *Am J Clin Nutr.* 2006; 84: 304-311.

18. Alvarado R, Alami RS, Hsu G, et al. The impact of preoperative weight loss in patients undergoing laparoscopic Roux-en-Y gastric bypass. *Obes Surg.* 2005; 15: 1282-1286.

19. Angulo P: Nonalcoholic fatty liver disease. *The New England Journal of Medicine.* 2002; 346: 16.1221–1231.

20. Zhu FS, Liu S, Chen XM, et al: Effects of n-3 polyunsaturated fatty acids from seal oils on nonalcoholic fatty liver disease associated with hyperlipidemia, *World Journal of Gastroenterology*. 2008; 14:41: 6395–6400.

21. Pagadala MR, McCullough AJ, The relevance of liver histology to predicting clinically meaningful outcomes in nonalcoholic steatohepatitis, *Clinics in Liver Disease*. 2012; 16: 3.487–504.

22. Lizardi-Cervera J, Aguilar-Zapata D: Nonalcoholic fatty liver disease and its association with cardiovascular disease. *Annals of Hepatology*. 2009; 8: 1.S40–S43.

23. Targher G, Day CP, Bonora E: Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. *The New England Journal of Medicine*. 2010; 363: 14. 1341–1350.

24. Bhatia LS, Curzen NP, Calder PC, et al: Non-alcoholic fatty liver disease: A new and important cardiovascular risk factor? *European Heart Journal*. 2012; 33: 10.1190–1200.

25. Targher G, Byrne CD: Nonalcoholic fatty liver disease: A novel cardiometabolic risk factor for type 2 diabetes and its complications. *Journal of Clinical Endocrinology and Metabolism*. 2013; 98: 2.483–495.

26. Argo CK, Northup PG, Al-Osaimi AMS, et al: Systematic review of risk factors for fibrosis progression in non-alcoholic steatohepatitis. *Journal of Hepatology.* 2009; 51: 2.371–379.

27. Chalasani N, Younossi Z, Lavine JE, et al: The diagnosis and management of non-alcoholic fatty liver disease: Practice guideline by the American Gastroenterological Association, American Association for the Study of Liver Diseases, and American College of Gastroenterology. *Gastroenterology*. 2012; 142: 7.1592–1609.

28. Levene AP, Goldin RD: The epidemiology, pathogenesis and histopathology of fatty liver disease. *Histopathology*. 2012; 61: 2.141–152.

29. Araya J, Rodrigo R, Videla LA, et al: Increase in long-chain polyunsaturated fatty acid n-6/n-3 ratio in relation to hepatic steatosis in patients with non-alcoholic fatty liver disease. *Clinical Science*. 2004; 106: 6.635–643.

30. K. Promrat, D. E. Kleiner, H. M. Niemeier et al: Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis, *Hepatology*. 2010; 51: 1.121–129.

31. Lazo M, Clark JM: The epidemiology of nonalcoholic fatty liver disease: A global perspective. *Seminars in Liver Disease*. 2008; 28: 4.339–350.

32. Simopoulos AP: Importance of the omega-6/ omega-3 balance in health and disease: evolutionary aspects of diet. *World Review of Nutrition and Dietetics*. 2011; 102: 10–21.

33. Kromhout D, Yasuda S, Geleijnse JM, et al: Fish oil and omega-3 fatty acids in cardiovascular disease: Do they really work? *European Heart Journal.* 2012; 33: 4.436–443.

34. Gloy VL, Briel M, Bhatt DL, et al: Bariatric surgery versus non-surgical treatment forobesity: A systematic review and meta-analysis of randomised controlled trials. s.l. *BMJ*. 2013; 347: f5934.

35. Sjostrom L: Review of the key results from the Swedish Obese Subjects (SOS) trial: A prospective controlled intervention study of bariatric surgery. s.l. *J Intern Med*. 2013; 273: 219–234.

36. Buchwald DM, Oien H: Metabolic/bariatric

surgery worldwide 2011. s.l. ***Obes Surg***. 2013; 23: 427–436.

37. Iannelli A, Martini F, Schneck AS, et al: Preoperative 4-week supplementation with omega-3 polyunsaturated fatty acids reduces liver volume and facilitates bariatric surgery in morbidly obese patients. ***Obes Surg.*** 2013; 23:1761–5

38. VanWissen J, Bakker N, Doodeman HJ, et al: Preoperative Methods to Reduce Liver Volume in Bariatric Surgery: A Systematic Review. ***Obes Surg.*** 2016; 26(2): 251-6.