BariClip-Jo

Assessing the safety and efficacy of the BariClip device in the treatment of severe obesity

IRB Protocol

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Introduction

Obesity and its associated disorders such as type 2 diabetes, nonalcoholic fatty liver disease, and cardiovascular disease have reached pandemic proportions worldwide. A recent survey of global trends found obesity was a cause of premature death in Europe (The Global BMI Mortality Collaboration Lancet 2016). The pooled data of almost 4 million people from 32 countries showed that people with higher BMI had an increased chance of death. For people with overweight or obesity, every additional five BMI points was linked to an additional 39% increase in their risk of death. Other notable results were:

- The increased risk of death linked to overweight or obesity was stronger at younger ages. The increased RR of death for every additional five BMI points over 25 was 52% for people aged 35 to 49 (HR 1.52, 95% CI 1.47 to 1.56), but 21% for people aged 70 to 89 (HR 1.21, 95% CI 1.17 to 1.25).
- Deaths from heart disease, stroke and respiratory disease were strongly increased for people with a BMI over 25, and death from cancer was moderately increased.

Similar findings had been derived from the Framingham database and the National Health and Nutrition Examination Survey (NHANES). In a Special Report in the New England Journal of Medicine (Olshansky NEJM 2005) Olshansky and colleagues argued that the increasing problems of obesity and its associated medical problems, will override the benefits of other health advances and a continued increase in life expectancy will not persist.

From these data we conclude that overweight and obesity is a health problem that leads to additional serious associated medical problems and a shortened life expectancy. Therefore, overweight and obesity deserves effective treatment.

Conventional medical care, even conducted by multidisciplinary teams combining dietary advice, physical activity and psychological treatment offers only limited results, both in weight reduction and reduction in obesity related problems. Bariatric surgery allows however, a significant and sustained weight loss in the majority of cases, and a decrease in the frequency and severity of associated medical problems, including type 2 diabetes, and decreased mortality including cardiovascular diseases. Whatever the technique proposed, it requires a major abdominal surgery associated with an estimated 5% significant perioperative morbidity and an average postoperative mortality estimated at 0.3%. Considered too invasive by many practitioners and patients, surgery is therefore proposed to a small proportion of patients who could theoretically benefit. The results of surgery have, however, validated the principle of the interventional treatment of obesity and its metabolic complications. This approach allows in particular to reduce or discontinue some treatments (oral agents, insulin, GLP-1 agonists, antihypertensive, lipid lowering) and limit their impact in terms of costs. However, still only a small percentage of the eligible candidates with severe obesity undergo bariatric surgery. In addition, whereas patients with severe obesity are eligible for bariatric surgery, the obesity epidemic mostly concerns relatively patients with less obesity relatively, with or without related medical problems, who do not meet the current bodyweight criteria for surgical therapy. In addition, the expanding obesity epidemic affects mostly individuals with less obesity relatively, who became eligible for bariatric surgery with the new 2022 IFSO/ASMBS joint guidelines. Hence, less invasive techniques and devices are rapidly being developed. These novel entities mimic several aspects of bariatric surgery either by gastric restriction (gastric balloons, gastric plication), by influencing gastric function (gastric botulinum injections, gastric pacing, and vagal

nerve stimulation), or by partial exclusion of the small intestine (duodenal-jejunal sleeve). In the last decade, several novel less invasive techniques have been introduced and some have been abandoned again. Endoscopic bariatric procedures are emerging techniques that are less invasive and safer compared with current surgical approaches. Since many of these novel techniques have not been investigated in randomized settings it is pivotal to thoroughly evaluate the effects, safety, long-term results, and reversibility of these mainly endoscopic techniques before clinical implementation.

A new device, which is basically a nonadjustable vertical clip, has been developed. This device, the BariClip, placed parallel to the lesser curvature, aims to restrict oral intake without changing the gastric or small bowel anatomy, requires no stapling, causes no malabsorption, does not require any maintenance or surveillance, and is reversible.

A prospective single arm clinical study will be conducted in Amman, Jordan at two different hospitals, Jordan Hospital and Al-Khalidi Medical Center, to assess the safety and efficacy of the BariClip procedure in the treatment of severe obesity.

The protocol of this study will be presented for approval to the IRB of the Jordan Hospital and Al-Khalidi Medical Center. The work will be carried out in accordance with The Code of Ethics of The World Medical Association (Declaration of Helsinki) for experiments involving humans and approved by the local committee.

The trial will be registered in the ISRCTN registry and a unique identification number (UIN) will be provided. The trial will be conducted according to the SPIRIT 2013 guidelines (Standard Protocol Items Recommendation for Interventional Trial).

The Clip

The Clip has a silicone-covered titanium base, except at hinge, designed to apply a low closing pressure (4.15gr/mm2) as measured intraoperatively with inner limb sensors when the Clip is closed and secured. It is 14.5 long, 11 mm wide, and fully flexible at the hinge – a 2.5cm inferior aperture. It opens flat and fits through a 12 mm trocar. It presents indentations with a Titanium rim for anchoring. It aims to restrict oral intake without changing the gastric or small bowel anatomy, requires no stapling, causes no malabsorption, does not require any maintenance or surveillance, and is reversible.

The Technique

The Clip is placed parallel to lesser curvature to separate the stomach into a restricted medial segment where food passes and an excluded larger lateral gastric segment. The inferior aperture aims at letting the gastric juices empty in their normal path. It also allows endoscopic visualization of the excluded stomach.

The Clip placement requires five trocars. The first step is to create a small opening at the angle of His with an articulated dissector, then a 3 to 4 cm window is created on the greater curvature, directly inferior to the incisura angularis. The articulated dissector is passed into the lesser sac to the left of the left gastric vessels and articulated to 90°, coming out at the angle of His. The Clip and its flexible closing belt is then inserted through this window via a 12 mm trocar and fixed to the stomach both anteriorly and posteriorly after inserting a calibration tube similarly as LSG (36 F bougie). The technique thus does not involve extensive dissection of the hiatus.

The patient is then checked with either intra-operative gastroscopy and/or postoperative Upper Gastrointestinal Swallow study using Gastrografin contrast material .

Previous Studies

Animal study

A pre-clinical animal study was conducted to support the safety and probability of effectiveness in humans and is briefly reported by Jacobs M et al (Obes Surg 2016).

The findings demonstrate that treatment with VPC limits weight gain in growing pigs compared with sham treatment group. The phase III survival study showed the mean weight gain of the pigs who underwent the sham surgery was almost 64% at 3 months, and the mean weight gain of the implant group was less than 10%. However, the number of animals evaluated at 3 months and the average weight gain in groups as well as the adverse events and the maximum duration of implantation are not reported.

Clinical Study

A clinical study was then conducted and included 117 patients who have been implanted with the Clip; the mean BMI at implantation was 44 kg/m^2 with a range from 35 to 56 kg/m^2. Following the implantation of VPC results appear favorable, with limited morbidity. As part of the European Union regulatory agencies requirements, 15 clips were removed after different lengths of time of implantation to prove reversibility. The choice and the data of these patients, after clip removal, were not reported. Since the VPC is a reversible device, the main concern is weight regain after removal. The decrease of numbers of patients in the long term follow up is explainable but the lowest frequency of follow up is not explained (at 3 months were 84/89, at 12 months were 61/70 month, at 18 months were 43/55 and at 24 months were 24/33). Limited long-term results are reported (24 months, 24/33 pts). The average percent excess weight loss at 24 months (%EWL) was 66.7% (47.73-84.21) and the mean weight loss 32.54 kg

(20.00-56.35 kg). No infections, transfusions, conversions, or deaths were encountered. The maximum duration of implantation is not reported. The quality of life following the implantation of the Clip was also studied and compared to the preoperative one via the BAROS questionnaire. It is the subject of an upcoming publication. Of the 82 patients who completed the questionnaires at all different points in time, the questionnaire showed failure for 1,2 % of patients and fair for 6,1 % of cases. The quality of life was assessed as good for 26 patients (31,8 %), as very good for 39 patients (47.5 %) and excellent in 11 patients (13.4 %), respectively. The potential benefits in terms of abdominal obesity, hyperglycemia, dyslipidemia, hypertension, sleep apnea and the changes in gastric hormones of appetite are not reported, and future high-quality long-term RCTs are needed to further assess efficacy and safety of the VPC for obesity. The first study has established the safety and efficacy of the BariClip, with a weight loss at 24 months is comparable to LSG. The incidence of GERD is significantly lower than after LSG. A few cases of slippage were most likely associated to an early device design and/or procedural learning curve. There has been only one case of erosion which is considered low versus the daily experience with LABG but is comparable with the predicated studies (US trial Lap Band study & US trial Realize Band). The BariClip can be safely removed with no major complications.

Study design

The clinical study is a prospective multicenter, single arm trial in which each subject serves as his or her own control. A precise blend of clinical patient genders, ethnic backgrounds, nationalities, age groups as well as social demographics, will be critical items considered during the patient selection process to gain a more universal insight to the results obtained from the study. A total of 50 patients will be enrolled in the study. The follow-up will be conducted at 1, 3, 6,12,18, 24, 36, 48, 60 months post implantation.

The final evaluation of the safety and efficacy of the Clip is to be based on a 60-month evaluation of the following clinical endpoints:

Primary endpoints:

1. % EWL: defined as weight loss divided by baseline excess weight. Excess weight will be determined from ideal body weight based on a BMI of 24.9 for normal adults (CDC – Center for Disease Control). By obtaining relevant data regarding the mean change in this variable, we can confidently draw conclusions about the expected baseline estimates of average effect in % EWL of the Clip.
2. Absolute Weight Loss: Defined simply as the total weight loss for the follow-up period.
3. Total Change in Weight (TWL%) defined as: (preoperative (preop) weight – follow up weight)/(preop weight) X 100%, measured at 12, 36 and 60 months
4. Total Change in BMI (TBMIL%) defined as (preoperative (preop) BMI – follow up BMI)/(preop BMI) X 100%, measured at 12, 36 and 60 months
5. Diabetic patients with the evolution of Plasma Glucose Levels, HbA1c levels, resolution of T2DM (% of patients).

Safety indicators and secondary endpoints:

1. Adverse events: incidence and severity of complications within 30 days and beyond 30 days. All classified according to Clavien-Dindo classification.
2. GERD and GI disturbances through GI Quality of Life (GIQLI) questionnaire: preoperative, at 12,36 and 60 months
3. Displacement on Contrast Imaging: After the procedure. Any significant displacement will be identified and reported.

The inclusion and exclusion criteria are as follow:

Inclusion criteria:

1. Age 18 – 65
2. Male or Female
3. BMI > 35 and BMI > 30 with at least one comorbid condition (HTN, DT2, Sleep Apnea…)
4. Willingness to comply with the substantial lifelong dietary restrictions required by the procedure (Written Consent Form)
5. History of failure with dieting methods
6. Willingness to follow protocol requirements including signed consent, routine follow-up schedule, completing QOL questionnaires, completing laboratory tests, completing diet and behavior modification counseling
7. Residing within a reasonable distance from an investigating center and able to travel to the investigator to complete all routine follow-up visits if not will schedule remote follow up through online platforms, such as Zoom with HIPPA compliance.

Exclusion criteria:

1. Surgery or treatment represents an unreasonable risk to the subject
2. Patient history of inflammatory disease of the GI tract (including ulceration, duodenal ulceration, grade 4 esophagitis, specific inflammation such as Crohn's disease or ulcerative colitis)
3. Severe cardiopulmonary disease or other serious organic disease
4. Severe coagulopathy, UGI bleeding conditions, such as esophageal or gastric varices, congenital or acquired intestinal telangiectasia
5. Congenital or acquired anomalies of the GI
6. Large hiatal hernia (> 4 cm)
7. Pregnant or has the intention of becoming pregnant in the next 12 months
8. Alcohol or drug addiction.
9. Mentally retarded or emotionally unstable, or exhibits psychological characteristics which, in the opinion of the investigators, make the subject a poor candidate for clip surgery
10. Previous esophageal, gastric surgery, hepatectomy, splenectomy
11. Previous endoscopic procedure for obesity
12. Patient under GLP1 medication or weight loss drug (Medication must be stopped 2 months prior at least)
13. Diabetes patient under treatment for gastroparesis
14. Previous bariatric surgery, intestinal obstruction, or adhesive peritonitis.

15. Patient history of a known diagnosis or pre-existing symptoms of systemic lupus erythematosus, scleroderma, or other autoimmune connective tissue disorder.
16. Participating in another ongoing clinical trial in which concomitant diagnosis or therapeutic intervention would adversely affect the integrity of the Clip clinical trial

A thorough assessment will be performed on patients, and will be divided on a routine screening, and a selective screening depending on patients' history and clinical presentation.

Routine screening:

1. Laboratory values
    a. CBC
    b. BMP (basic metabolic panel) or KFT (Kidney function)
    c. LFTs (liver function tests)
    d. Albumin
    e. HbA1c
    f. INR/PT/PTT
    g. TSH
    h. Vitamin B12, D
    i. Micronutrients
    j. Urine HCG (females)
2. Screening
    a. OSA
    b. Smoking

c. Substance abuse

d. QOL questionnaire

3. Consultations

    a. Nutrition

    b. Anesthesia

4. Testing

    a. Chest X Ray if indicated

    b. ECG if indicated

    c. Endoscopy (preoperative)

Selective screening:

1. Laboratory

    a. H. Pylori

2. Consultations

    a. Cardiology

    b. Endocrinology

    c. Gastroenterology

    d. Hematology

    e. Infectious diseases

    f. Nephrology

    g. ObGyn

    h. Orthopedics

    i. Pulmonary

j. Rheumatology

k. Sleep medicine

Similarly, the follow-up will be systemized and adapted depending on the patient's preoperative screening

Follow-up:

1. EWL, TBWL: 1 month, 3 months, 6 months, 12 months, 18 months, 24 months, 36, 48, 60 months
2. Annual blood work: CBC, KFT, LFT, Albumin, TSH, Hb A1c, Lipid profile, Vitamin & mineral panels
3. Endoscopy: Preoperative, 12, 36 and 60 months ~~an~~
4. GI series: day 1
5. Virtual Gastrography CT scan: 12, 36, and 60months
6. QOL and GIQLI questionnaires: Preoperative, 12, 36, and 60 months

Specific studies otherwise might be conducted if any health issue arises and are deemed necessary.

We intend to generate a publication after the trial is over. The trial will be registered in ClinicalTrials.gov.

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