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ORIGINAL ARTICLE

Laparoscopic sleeve gastrectomy in adolescents with or without syndromic obesity: two years follow-up

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Abstract
Introduction Childhood obesity is an emerging health problem. Surgical treatment of obese adolescents, particularly those affected by congenital syndrome, represents a controversial issue. The aim of this multicenter study was to retrospectively assess the results of laparoscopic sleeve gastrectomy (LSG) in a cohort of adolescents affected by morbid obesity, with or without congenital syndromes.
Materials and methods Forty-one obese (BMI 49 ± 6 kg/m^2) adolescents with mean age of 16 ± 3 years (58.5% with previous intragastric balloon failure), and subjected to LSG, were retrospectively evaluated for complications rate, % excess weight loss (%EWL), and inhibition of co-morbidities after 2 years of follow-up.
Results All the operations were completed laparoscopically and no intra-operative complications were recorded. No mortality was recorded while peri- or post-operative complications only occurred in two patients (4.9%). The EWL% at 6, 12, and 24 months were 42.3, 58.3, and 59.4, respectively. %EWL was comparable ($p = 0.7$) between non-syndromic and syndromic obese adolescents at 24 months. Conversely patients with previous intragastric balloon surgery had a significant lower EWL (%) at 24 month ($p < 0.01$). Moreover, at the same time point, co-morbidity resolution rate was 78.2% while improvement rate was 57.6%. Specifically, remission rate of type 2 diabetes (T2DM), hypertension and obstructive sleep apnea (OSA) were 71, 75 and 61%, respectively.
Conclusion LSG is advantageous in the treatment of morbidly obese juveniles concerning safety, weight loss and co-morbidity control and at same time presenting, a possible effective therapeutic option for patients affected by congenital syndrome.

Keywords Bariatric surgery in teenagers · Childhood obesity · Sleeve gastrectomy · Adolescents · Syndromic obesity · Surgical treatment

Introduction

Obesity is the fifth leading risk for global deaths. Childhood obesity is a growing public health problem with grievous long-term consequences. In last 30 years, the incidence of childhood obesity has been more than doubled in children and quadrupled in juveniles obese adolescents are more likely to suffer from several of co-morbidities, such as type 2 diabetes (T2DM), hypertension, nonalcoholic steatohepatitis (NASH), sleep apnea (OSA), and cholelithiasis. In addition, morbid obese adolescents will very likely become morbid obese adults [1–3]. Moreover, several studies have documented poor health-related quality of life (HRQL) in obese children, and the degree of obesity is related to the perceived impairments in emotional, social, physical, and school functioning. Based on the last US report, approximately 17% of children and teenagers (ages 2 to 19) were obese, 31.8% were either overweight or obese [3] and 6.5% of 12 to 19 year olds

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were morbidly obese [4]. In Italy, an overweight range between 14.9 and 40.6%, and obesity range between 2.4 and 19.5% have been reported, representing the highest incidence in Europe [5]. Etiology of childhood obesity is multifactorial and includes genetic, neuroendocrine, metabolic, psychological, environmental and socio-cultural factors. Constitutional obesity and mental retardation co-occur in several multiple congenital syndromes, including Prader–Willi (PWS), Bardet–Biedl, Cohen, Albright hereditary osteodystrophy, and Borjeson–Forssman–Lehmann syndrome as well as some rare disorders [6]. Bariatric surgery seems to offer, as in adult population, excellent result in adolescents, gaining progressive consensus in the scientific communities [7–10]. The ASMBS pediatric committee established in 2012 the selection criteria's for bariatric procedures in adolescents [11]. Further, a devoted position statement on bariatric surgery in adolescents was published by the Italian Society of Bariatric Surgery in 2009, which was subsequently confirmed in 2015 [12]. In the Fourth International Sleeve Gastrectomy Expert Panel Consensus Statement, 77% of the panelists identified the laparoscopic sleeve gastrectomy (LSG) as a valid treatment option in morbidly obese teenagers [13]. The purpose of this study was to evaluate the safety and effectiveness of LSG in morbid obese adolescents, with or without congenital syndromes, focusing on complications rate, weight loss and control of co-morbidities during 2 years of follow-up.

Methods

Definitions, inclusion and exclusion criteria

A multidisciplinary team consisting of a pediatric endocrinologist, two pediatric bariatric surgeons, three bariatric surgeons, two dieticians and a psychologist followed and assessed the patient's eligibility for bariatric surgery. The following inclusion criteria were applied: a body mass index (BMI) $\geq$35 kg/m^2 with major co-morbidities or >40 kg/m^2 with major/minor co-morbidities, failure to achieve a weight reduction after proved dietological treatment only, the presence of a dedicated caregiver from the patient's family, a supportive psychological evaluation in the form of behavioral, cognitive, emotional, and psychosocial assessments, motivation and realistic expectations by the patient and their family, the absence of contraindications for surgery, and informed consent or parental consent based on patient age [11]. The selected patients were included in an established program of pre-operative evaluation with bi-weekly appointment, followed by psychologists and registered dieticians for a period of 9 months, with constant and mandatory family support to guarantee the best medical management (reduced-energy diets with restricted access to food, regular physical activity), particularly in case of adolescents affected by syndromic obesity. The failure of this pre-surgical program was considered contraindications for surgery, as happened in six cases during our experience in the study period. Patients were screened for obesity related co-morbidities following national and international guidelines. Hypertension was defined as systolic or diastolic blood pressure that is higher than the 95th percentile for sex, age, and height on three or more pre-operative visits during the weight management period. Prehypertension was defined as systolic or diastolic blood pressure levels between the 90th and 95th percentiles for age, gender, and height according to the fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents [14]. Dyslipidemia was defined according to the report of the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents [15]. Diabetes and prediabetes were diagnosed according to the American Diabetes Association definition, which employed a cutoff point of 7.0 mmol/L for diabetes and 5.5 mmol/L for prediabetes [16]. Obstructive sleep apnea (OSA) and sleep-related breathing disorders were assessed clinically through the Pediatric Sleep Questionnaire (PSQ) and were investigated using polysomnography. OSA was diagnosed in patients who had an apnea/hypopnea index that was above 2 [17] and a PSQ score above 33 [18]. The diagnosis of polycystic ovarian syndrome (PCOS) was established according to the criteria derived from the 1990 National Institute of Child Health and Human Development (NICHD) conference and revised in 2003 [19, 20].

Resolution of all co-morbidities was evaluated clinically and biochemically at each follow-up visit. Remission of diabetes mellitus was defined as attaining a sustained FPG level below 7.0 mmol/L, and HbA1c level below 6.5% while not on anti-diabetes medication [16]. On the other hand, improvement of diabetes was defined as a decrease in FPG and/or HbA1c with outreaching normal levels, and/or a decrease in the dose or frequency of anti-diabetes medications [16]. For dyslipidemia, a level less than 2.8 mmol/L for LDL and more than 1.2 mmol/L for HDL were considered as remission, and remission of hypertriglyceridemia was defined as reaching a value within normal range for age (below 0.8 mmol/L for children below 10 years of age, or below 1.0 mmol/L for those 10 years of age and older) [15]. With regards to OSA, improvement and remission were evaluated based on change in the symptoms collected by the PSQ and finally with polysomnography, when needed [17, 18]. With regards to PCOS, improvement and remission were evaluated clinically based on normalization of menstrual disorders and the absence of signs of hyperandrogenism together with the

variation of medications dosage. In case of hepatic steatosis and/or nonalcoholic steatohepatitis (pre-operatively diagnosed), the diagnosis was confirmed intra-operatively with surgical biopsy, managed post-operatively with ultrasound at six months (finally every six months) and, in selected cases (severe NASH), re-evaluated with needle-biopsy ultrasound-guided. Chronic disease (cardiac, renal, pulmonary) was evaluated by the specialist team, considering the medications dose reduction as criteria of co-morbidities improvement.

Patients

Forty-one records of adolescent patients (20 male and 21 female) with mean age of 16 ± 3 years, a minimum follow-up of 24 months, and meeting the inclusion and exclusion criteria, were extracted from the prospectively maintained databases of the institutions involved in this study. All the patients affected by morbid obesity with mean pre-operative BMI 49 ± 6 kg/m^2 (range 39.2–69 kg/m^2) and mean excess weight of 75 ± 18 kg, were subjected to LSG. Seven of these (17.1%) were affected by syndromic obesity, six PWS and one Bardet–Biedl and complicated by severe co-morbidities requiring several hospitalizations. The others were all affected by co-morbidities (77% major). The PWS received neurologic treatment at least for 1 year (two patients with anticonvulsant therapy and selective serotonin reuptake inhibitor (SSRI); to piramate and fluoxetine) and were compliant with the scheduled neurologic and psychiatric treatment.

In 24 of these (58.5%), the first approach was an integrated management of dietician/psychologist support plus BioEnterics Intragastric Balloon (BIB) placement, but this was successful only in a 3% (criteria for success was = excess weight loss (EWL) >10% at 6 months). The majority of the surgical operation was performed in the pediatric hospital (33 patients, 80.5%) with daily round of multidisciplinary group, including bariatric surgeons, to guarantee specific and expert support during the hospital stay. The remaining 8 patients (19.5%, age 19) were treated in the bariatric center with final pre-discharge pediatric consultation.

Surgical interventions and post-operative management

LSG was carried out on calibrated 40 Fr bougie, starting 6 cm from pylorus using all reinforced cartridges (synthetic glycolide-trimethylene carbonate copolymer Gore®-Seamguard® Bioabsorbable Staple Line Reinforcement) and obtaining a final sleeve capacity of 90–100 ml (measured intra-operatively during blue methylene test). The abdominal drain was placed in 37 out of 41 patients (90.2%). No nasogastric tube was placed. Three cases required a posterior cruroplasty with non-absorbable stitches (hiatal hernia repair = HHR) for intra-operative finding of hiatal defects (7.3%). Methylene blue test, on the first and second post-operative day (37/41 patients, 90.2%), or X-ray with soluble oral contrast (Gastrografin®) (4/41 patients, 9.8%) were performed as leak test before clear liquid was started. The follow-up visits were scheduled at 1, 3, 6, 9, 12 months and then in every 6 months. In case of syndromic obesity, LSG was performed with the intention to be the first step of biliopancreatic diversion duodenal-switch (BPD-DS) and the decision to proceed to the second stage was evaluated case by case after a minimum follow-up of 12 months. Moreover, this group of the patients was also examined by the pediatric psychologist who was present in the office at each post-operative visit.

Data analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences, version 21.0 (SPSS, Inc., Chicago, IL). Descriptive statistics for continuous variables are presented as mean ± standard deviation. Categorical data are presented as counts and percentages. The following parameters were evaluated as percentages: conversion rate, intra-operative complications, operative time, hospital stay, peri- and post-operative complications (classified according to the Clavien–Dindo scores) [21], EWL, co-morbidities results (remission, improvement or unmodified). At two-year time point, descriptive and comparative analysis was performed between the entire study population, the patients affected by syndromic obesity and the patients with previous history of BIB. Statistical significance was set at $p < 0.05$.

Results

Anthropometric and clinical characteristics of the study population are reported in Table 1. All the operations were completed laparoscopically, and no intra-operative complications were recorded. The mean operative time was 94 ± 35 min. The average post-operative hospital stay was 5.3 ± 2 days. Statistically, significant difference was recorded between the hospital stay of patients with syndromic obesity, 9 ± 3 days vs. 4.2 ± 1.6 days for non-syndromic patients ($p < 0.05$). No incidence of mortality was recorded. Peri- or post-operative complications did occur in two patients (4.9%). First patient was subjected to LSG + HHR procedure and developed a transient dysphagia (score II) in the first week post-operative. Dysphagia was resolved after 50 days of conservative management (dietician counseling), prokinetic drug and a

Table 1 Demographics characteristics of study group

Number of patients (*N*)	41
Sex (M/F)	20/21
Age (mean ± SD)	15 ± 4.8 years
Syndromic obesity (*N*; type)	7; 6 Prader–Willi-1 Bardet–Biedl
Pre-operative BMI (mean ± SD)	49 ± 6 kg/m^2
Pre-operative BIB placement (*N*/%)	24/58.5%
Patients with major co-morbidities (*N*/%)	31/77%
Patients with minor co-morbidities (*N*/%)	10/23%

SD standard deviations

Table 2 Operative outcomes

LSG + HHR (*N*/%)	3/7.3%
Operative time	94 ± 35 min
Conversion rate (*N*/%)	0/0%
Intra-operative complications (*N*/%)	0/0%
Hospital stay (mean ± SD)	5.3 ± 2 days
Peri-/post-operative complications (*N*/%/Clavien–Dindo Score)	2/4.9%/II–IIIb

HHR hiatal hernia repair with posterior cruroplasty

full dose of proton-pump inhibitors (PPIs) The second patient, with pre-operative BMI of 68 kg/m^2, developed a trocar site hernia (2.3 cm^2 at 12 mm trocar site) 8 months after surgery (score IIIb) requiring an elective open repair, without post-operative complications (all the port access >10 mm were closed at the end of the primary procedure with Endo Close™ devices). Two patients required laparoscopic cholecystectomy 14 months and 20 months after LSG for symptomatic gallstones (4.8%) instead of prophylactic treatment with ursodeoxycholic acid (UDCA) as recommend by the review and meta-analysis published in 2008 [22]. The surgical outcomes are reported in Table 2. The average post-operative BMI was 42.8 ± 12, 40.3 ± 9, 39.5 ± 7, 32.3 ± 10, 32.8 ± 5, 31.3 ± 8, and 29.4 ± 13 kg/m^2 at 1, 3, 6, 9, 12, 18, and 24 months, respectively. At the same post-operative time, the EWL% were 17 ± 5, 30.1 ± 11, 42.3 ± 9, 51.5 ± 15, 58.3 ± 8, 59.6 ± 12, and 59.4 ± 6 as shown in Fig. 1. Regarding the co-morbidities, for T2DM, hypertension and OSAS the following results were obtained and presented as remission/improvement/unmodified: 71/29/0% (T2DM), 75/20/5% (Hypertension), 61/27/12% (OSAS). The mean resolution rate of the single co-morbidity, including the previously described, was 78.2%. The Fig. 2 represents the results of LSG on single co-morbidity. At two-year follow-up, the syndromic group patients (7–17.01%; mean age: 16.4 ± 2.7 years, mean pre-operative BMI = 47.3 ± 5.6 kg/m^2 and excess weight = 70.6 ± 20 kg) had an average %EWL of 15 ± 4, 26.7 ± 2, 37.8 ± 6, 48.8 ± 12, 56.6 ± 9 and 58.3 ± 8% after 1, 3, 6, 9, 12, and 24 months, respectively, and the value at two year was comparable with the entire population ($p = 0.7$) (Fig. 3). The psychiatrist reduced the drug dosage (topiramate from a mean dosage of 210.25 mg to a mean dosage of 85 mg at bedtime and fluoxetine to 10 mg/day to 0 at mean post-operative time of 16 ± 4 months) parallel the good compliance to follow-up schedule and family report of eating pattern which appeared substantially improved. The patients with previous history of BIB placement (24–58.5%; mean

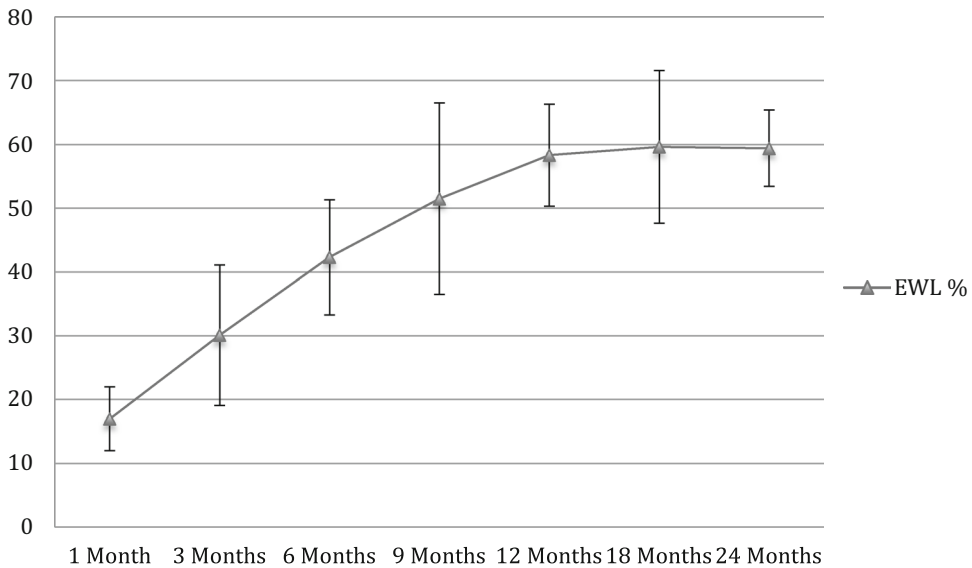

Fig. 1 Graph demonstrating EWL% evolution in post-operative follow-up (mean ± SD)

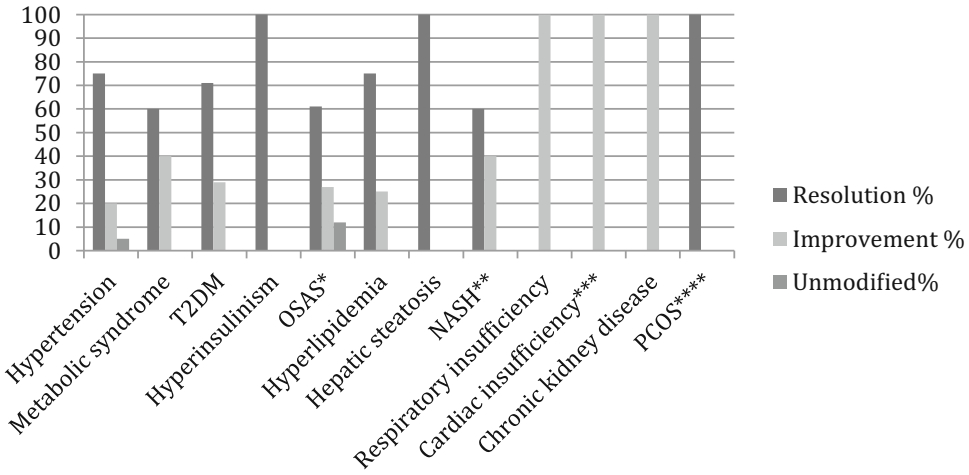

Fig. 2 Comparison of resolved, improved and unmodified co-morbidities. *Obstructive sleep apnea syndrome; **Nonalcoholic steatohepatitis; ***Previous valvular surgery; ****Polycystic ovarian syndrome

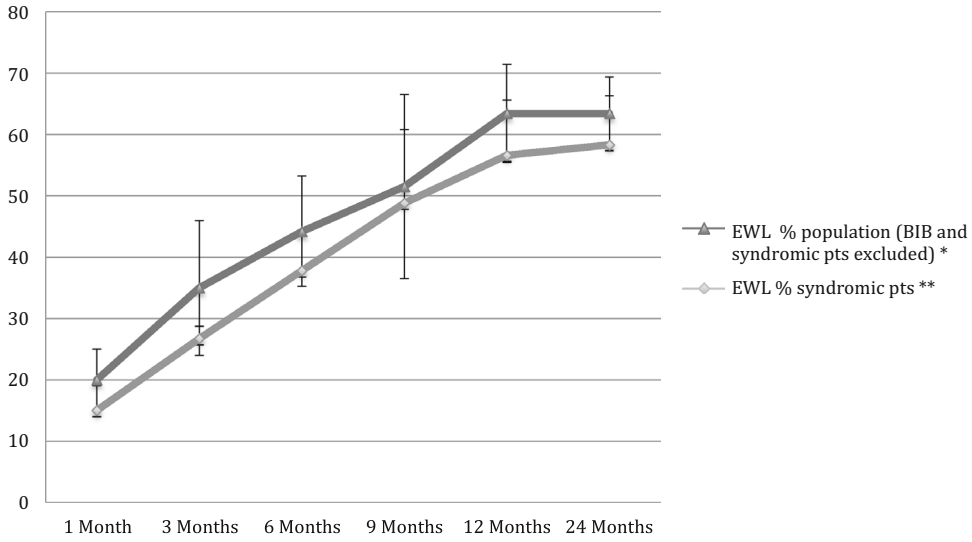

Fig. 3 Comparison of %EWL at 2 year of follow-up. Difference population* vs syndromic patient**; $p = 0.7$

age: 18.2 ± 3.2 years, mean pre-operative BMI: 45 ± 3.7 kg/m^2 and excess weight: 76 ± 17.3 kg) showed a mean %EWL of 13.5 ± 8, 28.3 ± 7, 36.5 ± 8, 43.7 ± 11, 51.3 ± 16 and 47.3 ± 9 after 1, 3, 6, 9, 12, and 24 months, respectively, and the value at two year was considerably lower compared to the entire population ($p < 0.01$) (Fig. 4). After 2 years of follow-up, four patients (9.7%; 2 patients with PWS) had an insufficient weight loss (IWL = EWL <50%) had remission of co-morbidities and are at present re-evaluated by the team for surgical revision.

Discussion

The most effective option for adolescent morbid obese it remains the surgical treatment. As reported in a recently published review and meta-analysis, laparoscopic gastric bypass (LGBP), LSG and laparoscopic adjustable gastric banding (LAGB) remains the three surgical options [8], considering malabsorbitive operation as potentially dangerous during this growing phase of life, and therefore non-indicated. The LGBP seems to be powerful concerning BMI loss and co-morbidities control (T2DM resolution in 79–100% of total series) [8] but has a complications rate (5.1% peri-operative, 17.1% re-intervention rate) higher than the LSG and LAGB. Moreover, the iron, vitamin A, B, D, folic acid, and zinc deficiencies together with the presence of a blind stomach remain the major limitation of the procedure. LAGB is a potential option for lower complication rate but less BMI loss compared with LGBP and LSG [9] and the presence of foreign bodies, requiring lifelong controls, regulation and possible re-operations, thus representing the limit of this procedure. Furthermore, a recent comparative publication between LSG and LGBP in late adolescents (65 patients/18–20 years; 45 subjected

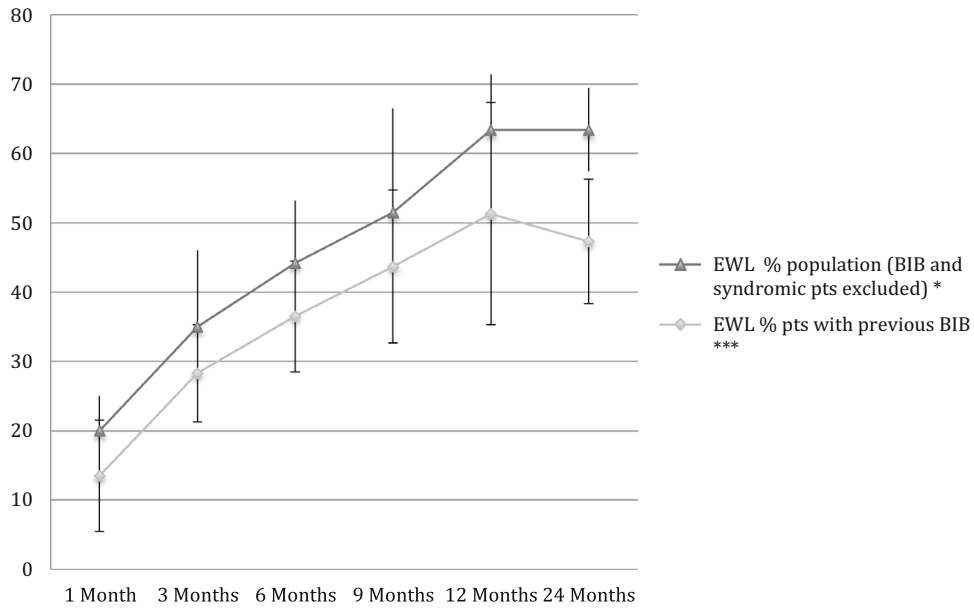

Fig. 4 Comparison of %EWL at 2 year of follow-up. Difference population* vs pts with previous BIB***; $p < 0.01$

to LSG and 20 to LGBP) showed a significant difference in %EWL at 2-year follow-up; 81.0% in LGBP versus 96.8% in LSG group without differences in complications rate [23]. Currently, LSG is the most diffuse procedures, in adult patients, and has higher growing rate worldwide [24]. The first review evaluating LSG in adolescents was published in 2013, analyzing 198 patients from nine studies. The review reports a percentage change in mean weight loss of 31.2% at 24 months, with total co-morbidity resolution rate of 70% in the absence of major complications [25]. Raziel et al. published their experience with 32 juveniles (age 14–18 years), on whom LSG was performed. The authors reported an average EWL of 81.7% after 1 year (15 patients) with concomitant resolution of co-morbidities in 82.4% of these and improvement in the others and a complication rate of 6.5% (one staple line leak and one acute cholecystitis) [26]. In the same year, Nocca et al. published a retrospective review where LSG was performed on 61 teenagers. An EWL of 66.7 and 78.4% after 1 and 2 years post-operation, respectively, (52.4% of the group) with co-morbidity resolution rate of 77.8% and complication rate of 19% (4 cases) was observed [27]. In the same year, Alqahtani et al. showed in 115 adolescents (age 13–17 years) and 37 young adults (age 18–21 years) a co-morbidity resolution or improvement, in 90.3% after 2 years without recurrence up to 3 years post surgery [28]. In 2015, Al-Sabah retrospectively evaluated 135 teenagers (age 12–21 years) subjected to LSG. Two years post surgery, a EWL of 84.7% with excellent results in co-morbidities resolution (100% T2DM and 75% hypertension) and a complication rate of 4.4% (6 cases) were noted [29]. Recently, Tsamis et al. confirmed the attractiveness of LSG in juveniles and young adults. They obtained an EWL of 81 ± 17%, EBMIL of 96 ± 21%, and BMI difference of −18.08 ± 4.38 kg/m^2 with complete remission of co-morbidities (100% after 3–6 months post surgery) [30]. All these studies conclude that LSG is an attractive therapeutic option for young patients. Our results furthers it by adding the safety and effectiveness along with attractiveness of LSG in adolescents and their families who affected by severe co-morbidities (77% major, 23% minor). This study indicates favorable results in terms of weight control (mean % EWL of 58.3 at 1 year and 59.4 at 2 years), with excellent outcomes in severe co-morbidity control (57.6%) and resolution (78.2%). The attractiveness was also emphasized by only two cases of low-grade complications (4.9%) with scores II and III b, confirming that the management of high-risk patients in a dedicated setting reduces dramatically the incidence of complications. Despite these encouraging results for obese adolescent, bariatric surgery and LSG remain absolutely controversial for syndromic obese adolescent, particularly in patients affected by PWS. Scheimann et al. concluded in their review that there is little justification for subjecting PWS patients to the potential risks of surgical interventions, thus supporting an alternative conservative approach [31]. The major limitations of the study by Scheimann et al. are principally related to the follow-up period, to completely abandoned or not more recommended procedures for adolescents. The lack of effective therapeutic interventions for adolescent with monogenic and syndromic forms of obesity exposes children in this group to significant morbidity and mortality secondary to severe obesity and associated conditions they are prone to develop [32]. In our experience, bariatric

surgery presents a hope for such children and should be highly considered. Our data indicated significant differences in hospital stay for syndromic and non-syndromic patients (9 ± 3 days vs 4.2 ± 1.6 days; $p < 0.05$) which is justified by different time needed to support the re-introduction of oral intake and to manage a particular category of patients with higher risk of surgical complications related to dysautonomia, decreased ability to vomit with risk of gastric rupture, the absence of fever during infectious episodes, and altered pain threshold that may delay the diagnosis of the complications [33]. Similar to other larger studies [34, 35], the %EWL of syndromic obese recorded after 2 years post surgery in our study, did not show any difference compared with the study population (58.3 vs. 63.4; $p = 0.7$). The evidence of two cases of IWL, even without co-morbidities relapse, suggests the possibility to adopt the two-step strategy and postpone the second stage of BPD-DS in adult age.

The effect of LSG in PWS patients regarding excellent weight results in the medium follow-up [34, 35] could be explained considering the macronutrient regulation, Ghrelin and Peptide YY (PYY), in patients affected by this congenital syndrome. As demonstrated by Balikcioglu et al. these patients have fasting and postprandial hyper ghrelinoma and an attenuated PYY response to fat, yielding a high Ghrelin/PYY ratio [36]. Considering the hormonal mechanism of LSG, reduction of Ghrelin level and high postprandial PYY response [37], this consideration should theoretically explain our excellent results, which is not remarkably different from the non-syndromic population.

Another concern raised from our data is related to the adolescents with previous history of BIB failure, an endoscopic obesity treatment largely approved as reduced-risk strategy. In our experience, the patients with previous BIB placement have a significant lower %EWL (47.3 vs 63.4%; $p < 0.01$), probably related to an adaptation of patients to restrictive procedure and this results should be discussed with the patients pre-operatively.

Despite reduction in excess weight loss, in high-risk adolescents patients with super obesity, obtain an excellent co-morbidities control seems to be the prior goal of the procedure, per se offering the chance of future possible revision (bridge procedure).

The major limitations of this study are related to the retrospective analysis, limited number of syndromic adolescents and the follow-up period.

Conclusions

In conclusion, LSG appears to be safe and effective treatment procedure primarily for weight loss and co-morbidity control in morbid obese teenagers. Further, results in syndromic adolescents support the two-stage strategy. The multidisciplinary approach is crucial to reach the optimal outcomes. Long-term data on a larger population are needed to better define the role of LSG in this category of patients and to confirm the effects in adults.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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