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Long-term effect of weight loss induced by bariatric surgery on asthma control and health related quality of life in asthmatic patients with severe obesity: A pilot study

Mauro Maniscalco [a, *], Alessandro Sanduzzi Zamparelli [b], Dino Franco Vitale [c], Stanislao Faraone [d], Antonio Molino [b], Anna Zedda [d], Andrea Motta [e]

[a] Pulmonary Rehabilitation Unit, ICS Maugeri SpA SB, Institute of Telese Terme, Benevento, Italy
[b] Department of Respiratory Medicine, A.O. dei Colli, University of Naples Federico II, Naples, Italy
[c] Clinical Epidemiology Section, ICS Maugeri SpA SB, Institute of Telese Terme, Benevento, Italy
[d] Section of Respiratory Medicine, Hospital S. Maria della Pietà, Casoria, Naples, Italy
[e] Institute of Biomolecular Chemistry, National Research Council, Pozzuoli, Naples, Italy

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ABSTRACT

Background: The weight loss induced by bariatric surgery (BS) improves asthma clinical control evaluated usually after a short time. The long-term effects of weight loss attained by BS on asthma control and health related-quality of life (HRQoL) in patients affected by asthma and obesity are not known.
Objective: To investigate the five-year effect of weight reduction induced by BS on asthma control, quality of life and pulmonary functional parameters in severely obese intermittent or mild-to-moderate asthmatic patients.
Methods: Twenty-six consecutive severe obese subjects with previous diagnosis of asthma with indication for laparoscopic adjustable gastric banding (LAGB) were enrolled into the study. Fifteen of them agreed to undertake the surgery (treatment group, TG) while the remaining eleven non-operated patients represented the control group (CG). Body mass index (BMI), Asthma Control Test (ACT), Mini Asthma Quality of Life Questionnaire (mini-AQLQ) and spirometric parameters were evaluated at baseline and after one and five years from surgery.
Results: Mean BMI of TG significantly decreased at one and five years after the surgery, while it remained unchanged in CG. After surgery, both the overall ACT and the mini-AQLQ score significantly improved in TG after one year, persisting improved after 5-years ($p < 0.001$), while these outcomes remained unchanged in CG. As compared with the pre-surgery values, the percentage of predicted FEV_1 and FVC significantly increased at five-year follow-up from surgery in TG, while it remained unchanged in CG.
Conclusions: In severe obese asthmatic patients, the significant improvement of asthma control test and HRQoL, observed one year after LAGB, persists five years after surgery.

1. Introduction

Obesity is a global problem, with several effects on the respiratory system, predisposing to serious respiratory diseases, including asthma [1]. Several epidemiological studies have reported the association between obesity and asthma [2–4], indicating an increase in asthma severity and exacerbation [5–7], therefore burdening patient's quality of life [8] and asthma control [9,10]. Recently, the respiratory metabolic phenotype (also called "metabotype") of obese asthmatic patients has been investigated by metabolomics [11,12]. It was demonstrated that asthma associated with obesity express a respiratory metabotype that is fully different, not summatory, with respect to those separately characterizing patients with either asthma or obesity alone.

Weight loss may improve lung function, asthma control and

Abbreviations: ACT, Asthma control test; AQLQ, Asthma Quality of Life Questionnaire; BMI, body mass index; CG, control group; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HRQoL, health related-quality of life; LAGB, laparoscopic adjustable gastric banding; PFTs, pulmonary function test measurements; TG, treatment group.

* Corresponding author. Via Bagni Vecchi 1, 82037, Telese Terme, BN, Italy.
E-mail address: mauromaniscalco@hotmail.com (M. Maniscalco).

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severity in adult obese asthmatics [13–16]. In particular, weight loss induced by bariatric surgery appears to be an effective tool to improve asthma control and symptoms, although the effect has been usually evaluated after a relatively short period [15,17–20]. Accordingly, in a one-year prospective study we demonstrated an improvement in asthma control and lung function in a group of asthmatic obese patients after weight lost induced by surgical treatment [21]. The few long-term studies (≥5 years) published so far evaluated only the percentage of asthma resolution, without considering symptoms, control or functional parameters [19,22,23]. In particular, the persistence or the reversibility of the effect induced by weight loss after long term from the bariatric surgery is not known.

In this paper, we investigated the long-term (five-year) effects of weight loss induced by bariatric surgery on asthma control and the health-related quality of life (HRQoL) and lung function in severe obese asthmatic patients.

2. Materials and methods

2.1. Patients

Twenty-six consecutive severe obese subjects with previous diagnosis of intermittent or mild-to-moderate asthma attending our bariatric surgery clinic (tertiary care) for laparoscopic adjustable gastric banding (LAGB) evaluation were enrolled into the study from April 2010 to April 2011. Fifteen of them agreed to undertake the surgery (treatment group, TG), while the remaining eleven, which refused for reasons unrelated to asthma or other health problems, represented the control group (CG).

All patients were non-smoker or had stopped smoking for two years or more. The diagnosis of asthma was made following the American Thoracic Society criteria [24]. Atopy was based on positive wheal responses (>3 mm) to 12 common airborne allergen extracts (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* and dog and cat dander), pollens (*Gramineae*, *Parietaria* species, *Betulaceae*, *Artemisia* and *Oleaceae),* and mould *(Aspergillus, Alternaria and Cladosporium)* using a standardized skin prick test kit (Allergopharma Hamburg, Germany). Exclusion criteria included the following: cardio-respiratory disturbances, obstructive sleep apnea, and history of upper respiratory tract infection or relevant allergen exposure within 4 weeks before entering the study.

The local Ethics Committee approved the study protocol and informed written consent was obtained.

2.2. Outcomes

Six outcome parameters were considered. The Body Mass Index (BMI), the Asthma Control Test (ACT), the Mini Asthma Quality of Life Questionnaire (Mini-AQLQ) and three pulmonary functions (PFTs) (FEV_1, FVC, FEV_1/FVC).

2.3. Pulmonary function test measurements

Flow rates were determined using automated equipment (V Max 22 System SensorMedics, Milan, Italy). Forced inspiratory and expiratory maneuvers were performed three times and the best value obtained from the maximum inspiratory and expiratory flow-volume curves were used for comparison. Recommendations for standardized procedures for various lung function tests were followed [25].

2.4. Asthma control and HRQoL

To assess the asthma control and HRQoL we used the ACT and the mini-AQLQ, respectively. The ACT consists of five questions, each with a five-point scale assessing asthma symptoms (daytime and nocturnal), use of rescue medications, and the effect of asthma on daily functioning [26]. The score ranges from 5 to 25, with lower scores indicating poorer asthma control. Subjects with an ACT score <20 were defined as having not well-controlled asthma. The mini-AQLQ consists of 15 questions on symptoms, activity limitations, emotional function and environmental stimuli, each with a 7-point scale [27]. The score ranges from 1 to 7, with lower scores indicating poorer HRQoL.

2.5. Experimental procedure

The PFTs, ACT questionnaire and mini-AQLQ were performed before surgery, and repeated one and five years after the surgery in TG; at baseline and after one and five years in CG. All measurements were carried out at lunchtime. All subjects were fasted for 4 h before the tests. The subjects' weight and height were measured immediately before the start of the experiment. Patients with allergy to pollen were studied out of season. The dose and timing of long-acting β_2-agonists were identical at study visits before and after weight loss. Patients did not consume any short-acting bronchodilators for 4 h before pulmonary function tests.

2.6. Statistics

Continuous variables are expressed as mean ± standard deviation (SD) while categorical variables are expressed as rates. To evaluate the effect of the treatment at each follow-up time and the possible changes between follow-up times in each treatment group, we performed a multiple regression using as dependent variables the differences between each follow-up time and the baseline of each outcome. Being aware that the errors of the multiple (six) regression models have a great probability of being correlated, we analyzed our data by applying a “seemingly unrelated regression” model (SUR) [28] with the relative multivariate analysis of covariance (MANCOVA) (see Supplemental Data). A one-way multiple analysis of variance (MANOVA) model was used to test the differences on baseline parameters between the group of patients undergoing surgery and the control group. A one-way analysis of variance (ANOVA) on the items composing the ACT and mini-AQLQ scores changes was employed to assess whether changes observed in the global scores were attributable to one or more specific item. Data were analyzed by Stata version 13.0 (StataCorp LP, College Station, Texas). Statistical significance was accepted at $p < 0.05$.

3. Results

Baseline characteristics of patients are shown in Table 1. No significant differences were observed on baseline values of age and the six outcome variables between treatment and control groups ($p = 0.26$). Furthermore, no significant differential behavior in any of the items composing the ACT and the mini-AQLQ global score was observed between the two groups (always $p > 0.6$; Table 2).

The MANCOVA analysis shows that the main effect of the surgery (treatment) is significant ($p \leq 0.0001$) without differences between the four statistics (Wilk's lambda, Lawley-Hoteling trace, Pillai's trace and Roy's largest root). While the main effect of the follow-up time is not significant ($p = 0.088$), its interaction with the surgery is significant ($p = 0.008$). Interestingly, the model includes a significant effect of age as confounder. The lack of significance of the follow-up time ($p = 0.088$) does not imply that significant differences related to follow-up cannot be observed since the interaction term is actually significant. Therefore, specific time