

The Link between Morbid Obesity and Sleep Apnea:

"Thou seest I have more flesh than
another man, and therefore more frailty."

Falstaff, Henry IV Part I, III.iii.170.

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Background:

Obstructive sleep apnea (OSA) is characterized by recurrent episodes of upper airway collapse and obstruction during sleep. These episodes of obstruction are associated with recurrent oxyhemoglobin desaturations and arousals from sleep. OSA associated with excessive daytime sleepiness (EDS) is commonly called obstructive sleep apnea-hypopnea syndrome (OSAHS).

Despite being a common disease, most primary care physicians in the United States underrecognize OSAHS; an estimated 80% of Americans with OSAHS are not diagnosed. Although its prevalence may vary in different populations and age groups, it has been estimated that OSA affects 24% and 9% of middle-aged men and women respectively (1). The prevalence of sleep apnea in young African Americans (<25 years of age) appears to be greater than in white Americans. Recent evidence indicates that the prevalence in older age groups is similar between African Americans and white Americans, but the OSA is more severe in African Americans (i.e. African Americans have higher AHI).

The male-to-female ratio in community-based studies is 2-3:1. Three large epidemiologic studies have demonstrated that the prevalence of OSA in women appears to increase after menopause (2, 3, and 4). Premenopausal women with OSA tend to be more obese than men with the same severity of disease. Thin women with symptoms of OSA appear to have an increased frequency of craniofacial abnormalities (5).

OSA is associated with systemic hypertension, pulmonary hypertension and cor pulmonale. Obesity is probably the most important risk factor for OSA. Several studies have shown an association between increased body mass index (BMI) and the risk of OSA (6). Significant OSA is present in 40% of obese individuals (7) and 70% of OSA patients are obese (7). A mere 10% increase in body mass has been shown to increase an individual's risk of developing OSA by 500% (8). Conversely, weight loss in OSA patients leads to a significant decrease in apnea frequency (figure 1).

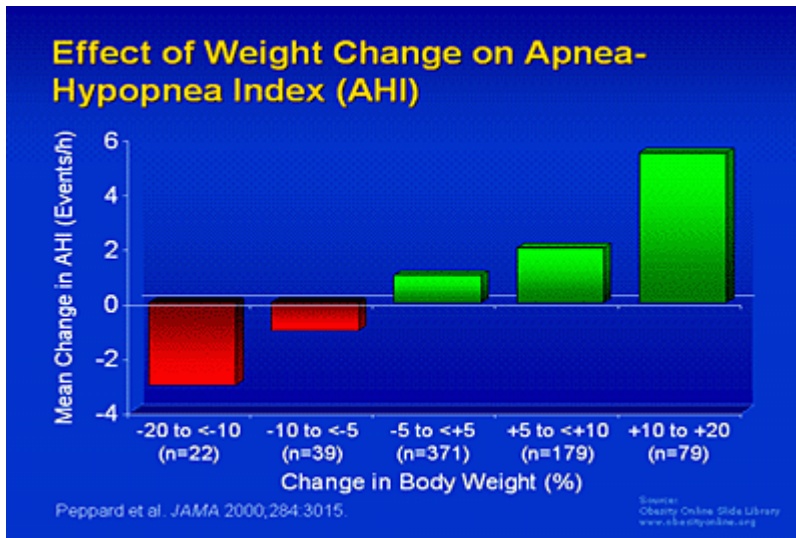


Figure 1
(Ref 8)

Pathophysiology:

Conceptually, the upper airway is a compliant tube and, therefore, is subject to collapse. Most patients with OSA demonstrate upper airway obstruction at either the level of the soft palate (i.e., nasopharynx) or the level of the tongue (i.e., oropharynx). Recent research indicates that both anatomic and neuromuscular factors are important. Anatomic factors, such as enlarged tonsils, macroglossia, or abnormal positioning of the maxilla and mandible, decrease the cross-sectional area of the upper airway and/or increase the pressure surrounding the airway, both of which predispose the airway to collapse. Upper airway neuromuscular activity, including reflex activity, decreases with sleep, and this decrease may be more pronounced in patients with OSA. Reduced ventilatory motor output to upper airway muscles is believed to be the critical initiating event leading to upper airway obstruction; this effect is most pronounced in patients with an upper airway predisposed to collapse for anatomical reasons.

Etiologic link between OSA and Obesity:

The exact mechanisms underlying the effects of obesity on the risk of OSA are still unclear. It may be related to effects of fat deposition on airway anatomy or changes in upper airway function. Weight loss has been shown to be associated with a decrease in upper airway collapsibility in OSA (9). Obesity-induced changes in central mechanisms regulating airway tone or ventilatory control stability may also be implicated. Leptin, for example, which is increased significantly in obesity, has important effects on regulation of chemoreflex function and hence breathing control (10).

Whereas obesity increases the risk for OSA, sleep apnea may predispose to weight gain and obesity. Indeed, patients with newly diagnosed OSA have a

history of excessive weight gain in the period preceding the diagnosis (11, 12). Furthermore, chronic CPAP treatment has been shown to reduce total body fat in patients with OSA.

The mechanism of this association is probably multifactorial. It may be related to changes in lifestyle, so that individuals with OSA may tend to gain weight because of daytime somnolence and a decrease in physical activity. Weight gain in OSA may also be related to endocrine dysregulation. Leptin, the protein product of the *ob* gene, is produced by adipocytes (13). Leptin suppresses appetite and increases energy expenditure, hence inducing weight loss. Obese individuals have high circulating leptin levels but exhibit end-organ resistance to its effects (14). Male patients with OSA have 50% higher plasma levels of leptin when compared to similarly obese control subjects with no sleep dysfunction (12). It is, therefore, likely that sleep apnea is accompanied by potentiated leptin resistance, so that the weight-reducing effects of leptin are blunted in OSA, hence predisposing to a cycle of weight gain and worsening OSA. Leptin may also alter respiratory control, thereby contributing to the disorders of breathing in obese, hyperleptinemic patients with OSA.

Treatment of OSA:

Medical care:

Treatment of severe obstructive sleep apnea is imperative because the associated mortality and morbidity are high. A hallmark study (15) showed that 40% of persons with an apnea-hypopnea index greater than 20 died over an 8-year period if untreated. The treatment of OSA in part depends on the severity of the sleep-disordered breathing. People with mild apnea have a wider variety of options, while people with moderate-to-severe apnea should be treated with nasal CPAP.

Conservative measures include weight loss, avoidance of alcohol for 4-6 hours prior to bedtime, and sleeping on one's side rather than on the stomach or back. Include these measures in the treatment of all patients with OSA, but use them only in patients with very mild apnea whose main symptom is snoring.

- Nasal CPAP: CPAP is the most effective treatment for OSA (16) and it has become the standard of care. CPAP works by splinting the upper airway, preventing the soft tissues from collapsing. By this mechanism, it effectively eliminates the apneas and/or hypopneas, decreases the arousals, and normalizes the oxygen saturation.
 - CPAP has been shown to improve daytime sleepiness, mood, and cognitive function in people with both mild and moderate apnea. CPAP has also been shown to increase quality of life and decrease health care costs. Data indicate that CPAP decreases blood

- pressure, primarily in patients with severe OSAHS (17). Evidence also indicates that it may improve the left ventricular ejection fraction in patients with congestive heart failure and OSAHS (18).
- The most common adverse effects of CPAP are dry mouth, rhinitis, and sinus congestion. These can be treated effectively with humidification and antihistamines and/or nasal steroids.
 - Unfortunately, compliance is a major problem, with only approximately 50% of patients using CPAP on a regular basis in short-term studies. Predictors of compliance include severe daytime sleepiness, baseline AHI, and a higher level of education.
 - Some patients require the use of bi-level positive airway pressure (BPAP). In BPAP, a higher inspiratory pressure and a lower expiratory pressure are used. In patients with sleep apnea, the levels are set such that the expiratory pressure eliminates apneas and the inspiratory pressure eliminates hypopneas. BPAP is generally used in patients who cannot tolerate high CPAP pressures (i.e., patients who experience difficult exhalations) or who have barotrauma complications (e.g., ear infections, bloating). Many laboratories automatically place a patient on BPAP if the CPAP level needs to be increased above 15 cm water. Compliance with BPAP has not been demonstrated to be better than compliance with CPAP.
- Oral appliances: These act by moving the tongue or mandible forward, enlarging the posterior airspace.
 - Oral appliances have been shown to decrease the AHI in most patients. However, they are most effective for patients with AHIs of less than 40 episodes per hour.
 - One study directly compared CPAP with oral appliance use in non-severe OSA. Considering all 20 subjects, after 6 weeks of treatment, normalization of the respiratory parameters was seen only with CPAP. The patients considered the ISAD to be easier to use and indicated greater utilization of the device in comparison with CPAP (19).
 - In summary, evidence suggests that oral appliances may be appropriate first-line therapy in people with mild apnea and can be used as an alternative for mild-to-moderate OSAHS if the patient does not tolerate CPAP.

Surgical Care:

Surgical correction of the upper airway is no longer considered primary therapy. Generally, surgery is recommended only for patients for whom CPAP was unsuccessful, for patients who refuse to consider CPAP, or for those who have very mild (i.e., AHI <10) OSAHS. Surgeries include the following:

- Uvulopalatopharyngoplasty (UVP₃) is resection of the uvula and soft palate. It is effective in approximately 40% of patients, but predicting which patients benefit from the procedure is impossible. The new laser-assisted approach should only be used for patients with simple snoring. Long-term, patients with a treatment success have a recurrence of symptoms.
- Craniofacial reconstruction involves advancement of the tongue (geniohyoid advancement with hyoid myotomy) or maxillomandibular bones (maxillomandibular osteotomy). These surgeries should be performed only at centers with expert personnel. Short-term success rates are approximately 70% for the geniohyoid advancement and 95% for maxillomandibular osteotomy. No good long-term studies of success have been conducted for these surgeries.
- Tracheostomy provides definitive correction because it bypasses the obstruction. It is recommended for patients with very severe OSAHS, especially if the patient does not tolerate CPAP or has cor pulmonale.

Bariatric surgery and OSA:

The Role of Surgery in Treating Severe Obesity

Surgery for morbid (clinically severe) obesity (BMI > 40) should be considered a treatment of last resort after dieting, exercise, psychotherapy, and drug treatments have all failed. The 1991 National Institutes of Health Consensus Conference on Gastrointestinal Surgery for Severe Obesity concluded that “patients whose BMIs exceed 40kg/m² are potential candidates for surgery if they desire substantial weight loss because obesity severely impairs the quality of their lives...” In certain instances, less severely obese patients (those with a BMI of between 35 and 40kg/m²) may also be considered for surgery. Included in this category are patients with high-risk comorbid conditions such as life-threatening cardiopulmonary problems (e.g. OSA) or severe diabetes mellitus (20).

There are a number of operations that have been used in the treatment of clinically severe obesity. They are known collectively as **bariatric** surgery, a term coined from the Greek words for *weight* and *treatment*. Approximately 140,000 weight-reduction procedures were performed in the USA in 2004 alone. The number of such procedures rose by 450 percent from 1998 to 2002. Eighty percent of the patients are women; most are middle-aged or younger.

The current gold standard for the surgical treatment of clinically severe obesity is the gastric bypass (GB) (figure 2). This operation was first performed for obesity over 30 years ago and was developed after surgeons observed massive weight loss in patients undergoing gastric surgery for ulcers or cancer. Approximately 75 percent of all operations performed for severe obesity in the U.S. are now of this type. A small pouch (around 30 cc or one fluid ounce in size) is created by

stapling across the top of the stomach, causing massive restriction in food intake. A section of the small intestine (two to five feet in length) is attached to it so that food can bypass the duodenum and the first portion of the small intestine, reducing calorie and fat absorption. The anastomosis from the gastric pouch to the jejunum is kept small (around 12mm) so that food and fluids can only pass very slowly into the intestine, again limiting the number of calories that can be absorbed from food at any one time.

Roux-en-Y Gastric Bypass

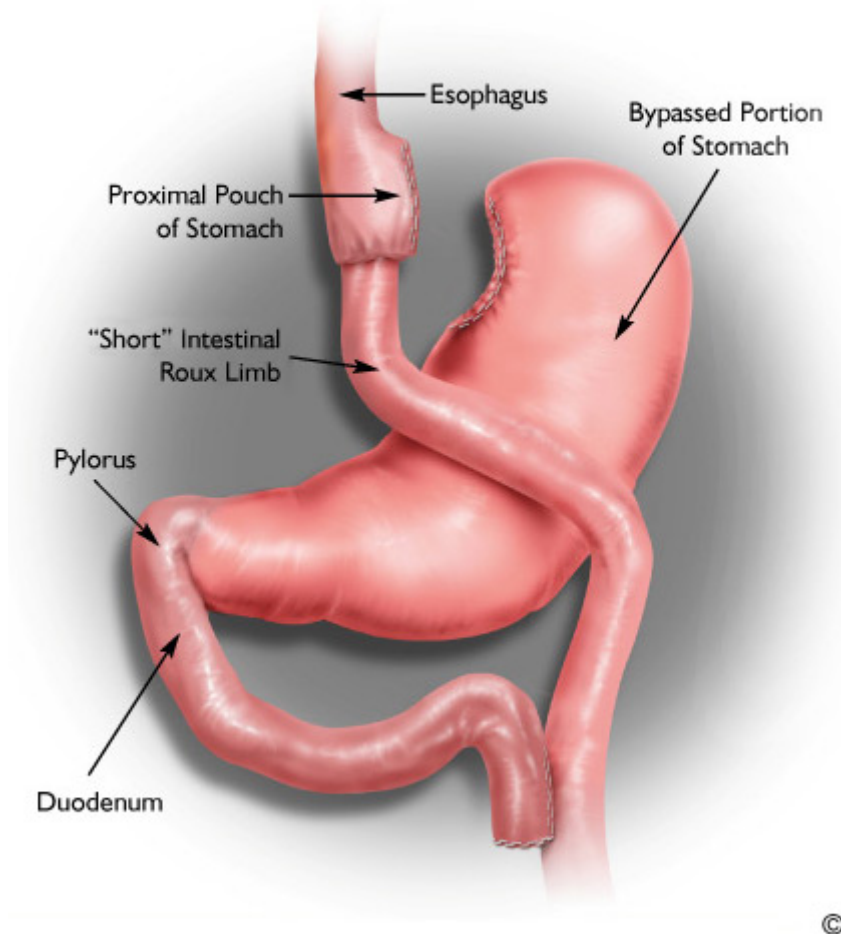


Figure 2

Most patients can expect to lose 67 percent of their excess weight 2 years after GB surgery (21). Long-term weight regain at nine years after surgery is approximately only 10-15% of initial weight loss (21).

Resolution of OSA after GB surgery:

Gastric bypass surgery not only induces significant weight loss in successful patients but also leads to marked improvements in associated co-morbidities. A recent survey demonstrated that obstructive sleep apnea (OSA) occurs in up to 60% of patients undergoing bariatric surgery. Rasheid and his group at the University of South Florida examined the effect of weight loss following bariatric surgery on OSA (22). 100 consecutive patients with symptoms of OSA were prospectively evaluated by polysomnography before gastric bypass. The investigators compared preoperative and postoperative scores of Epworth Sleepiness Scale (ESS), Respiratory Disturbance Index (RDI), and other parameters of sleep quality.

Preoperative RDI was 40 +/- 4 (normal 5 events/hour). 13 patients had no OSA, 29 had mild OSA, while the remaining 58 patients were treated preoperatively for moderate-severe OSA. At a median of 6 months follow-up, BMI and ESS scores improved (38 +/- 1 vs. 54 +/- 1 kg/m², 6 +/- 1 vs. 12 +/- 0.1, postoperatively vs. preoperatively). 11 patients completed postoperative polysomnography (3-21 months) after losing weight (postoperative BMI 40 +/- 2 vs. preoperative BMI 62 +/- 3 kg/m²). There was significant improvement in ESS (3 +/- 1 vs. 14 +/- 2), minimum O₂ saturation (SpO₂ 86 +/- 2 vs. 77 +/- 5), sleep efficiency (85 +/- 2% vs. 65 +/- 5%) and RDI (56 +/- 13 vs. 23 +/- 7, P = 0.041). Regression analysis demonstrated no correlation between preoperative BMI, ESS score and the severity of OSA; and no correlation between % excess body weight loss and postoperative RDI.

A similar study from Charuzi and colleagues compared sleep quality before and after bariatric surgery in 13 patients (23). Pretreatment polyhypnographic recordings of patients with SAS demonstrated considerable reduction of deep and rapid eye movement (REM) sleep stages with a correspondent prolongation of wake within sleep or non-REM sleep stages I and II. After surgical weight reduction, repeated polyhypnographic recordings revealed considerable improvement or even a complete recovery of breathing in sleep and a normalization of sleep structure. Non-REM deep sleep stages (III and IV) augmented from 5.51% +/- 2.53% (mean + SEM) to 22.69% +/- 3.56% and the REM stage increased from 9.91% +/- 1.78% to 18.15% +/- 2.13%.

Obesity hypoventilation syndrome (OHS: characterized by hypoxemia and hypercarbia while awake) is often associated with OSA. The Medical College of Virginia group showed that 126 (12.5%) of 1010 patients undergoing gastric bypass surgery demonstrated OSA and/or OHS (24). In the 12 patients in whom arterial blood gases were available > 5years after surgery, paO₂ increased from 54 +/- 10 to 68 +/- 20 mm Hg and paCO₂ fell from 53 +/- 9 to 47 +/- 11 mm Hg. Postoperative pulmonary function tests showed significant improvement in expiratory reserve volumes after surgery, suggesting improvement in the alveolar collapse and shunting during expiration typically seen in obesity-induced

restrictive lung disease. Sugerman's group also showed reductions in pulmonary artery pressures in OHS patients after surgery. These were typically elevated before surgery but normal 3-9 months after the procedure.

OSA as a risk factor for GB surgery:

Although morbidly obese patients with OSA can anticipate significant amelioration in their sleep condition after gastric bypass surgery, it is important to realize that their apnea does put them at a higher risk of postoperative complications when compared to patients with similar BMI but no OSA.

Ballentyne retrospectively reviewed the hospital records of 311 patients who underwent RYGBP in a 6-month period (25). He found that a preoperative history of OSA predicted a longer length of stay after GB surgery. Sugerman found that severe respiratory insufficiency of obesity (OSA+/-OHS) predicted a 2.4% perioperative mortality rate vs. 0.2% mortality in those patients with no significant pulmonary dysfunction.

The use of CPAP in the postoperative bariatric patient:

The use of CPAP has not been universally accepted for patients with OSA following upper gastrointestinal surgery because of concerns that pressurized air will inflate the stomach and proximal intestine, resulting in anastomotic disruption. A recent study was performed at UCLA to assess the safety and efficacy of postoperative CPAP for patients undergoing a gastrojejunostomy as part of a gastric bypass procedure (26). A total of 1067 patients (837 women [78%] and 230 men [22%]) were prospectively evaluated for the risk of developing anastomotic leaks and pulmonary complications after the GB procedure. Of the 1067 patients undergoing gastric bypass, 420 had obstructive sleep apnea and 159 were dependent on CPAP. There were 15 major anastomotic leaks, two of which occurred in CPAP-treated patients. Despite the theoretical risk of anastomotic injury from pressurized air delivered by CPAP, no anastomotic leaks occurred that were attributable to CPAP. A more recent study of 415 laparoscopic GB patients, 64 of whom had OSA, confirmed that routine use of CPAP after GB does not convey added risk of anastomotic disruption to patients with significant OSA (27).

Conclusion:

OSA is a serious medical condition, linked to systemic hypertension, pulmonary hypertension and cor pulmonale. Up to 24% of middle-aged men may be afflicted with this condition. The most significant risk factor for OSA is obesity. Alterations in the severity of the condition are closely linked to changes in an individual's weight.

Medical and surgical treatment of severe obesity improves associated OSA. The presence of OSA in patients undergoing bariatric surgery, however, significantly increases the incidence of morbidity and mortality in the postoperative period. The use of CPAP to treat OSA in the early postoperative period after gastric bypass surgery should be encouraged, since it can be safely administered and should reduce the incidence of pulmonary complications occurring after the procedure.

References:

- (1) Young, T, Palta, M, Dempsey, J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med*. 1993 Apr 29; 328(17):1230-5.
- (2) Hla, KM, Young, TB, Bidwell, T, et al: Sleep apnea and hypertension. A population-based study. *Ann Intern Med* 1994 Mar 1; 120(5): 382-8
- (3) Shahar, E, Whitney, CW, Redline, S, et al: Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2001 Jan; 163(1): 19-25
- (4) Young, T, Finn, L, Austin, D, Peterson, A: Menopausal status and sleep-disordered breathing in the Wisconsin Sleep Cohort Study. *Am J Respir Crit Care Med* 2003 May 1; 167(9): 1181-5
- (5) Guilleminault, C, Stoohs, R, Kim, YD, et al. Upper airway sleep-disordered breathing in women. *Ann Intern Med* 1995;122(7):493-501
- (6) Young, T, Peppard, PE, Taheri, S. Excess weight and sleep-disordered breathing. *J Appl Physiol*. 2005 Oct; 99(4):1592-9.
- (7) Vgontzas, AN, Tan, TL, Bixler, EO et al. Sleep apnea and sleep disruption in obese patients. *Arch Intern Med*. 1994 Aug 8; 154(15):1705-11.
- (8) Peppard, PE, Young, T, Palta, M et al. Longitudinal study of moderate weight change and sleep-disordered breathing. *JAMA*. 2000 Dec 20; 284(23):3015-21.
- (9) Schwartz, AR, Gold, AR, Schubert, N et al. Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis*. 1991 Sep; 144(3 Pt 1):494-8.
- (10) O'Donnell, CP, Tankersley, CG, Polotsky, VP et al. Leptin, obesity, and respiratory function. *Respir Physiol*. 2000 Feb; 119(2-3):163-70.
- (11) Phillips, BG, Hisel, TM, Kato, M et al. Recent weight gain in patients with newly diagnosed obstructive sleep apnea. *J Hypertens*. 1999 Sep; 17(9):1297-300.
- (12) Phillips, BG, Kato, M, Narkiewicz, K et al. Increases in leptin levels, sympathetic drive, and weight gain in obstructive sleep apnea. *Am J Physiol Heart Circ Physiol*. 2000 Jul; 279(1):H234-7.

- (13) Zhang, Y, Proenca, R, Maffei, M et al. Positional cloning of the mouse obese gene and its human homologue. *Nature*. 1994 Dec 1; 372(6505):425-32.
- (14) Considine, RV, Sinha, MK, Heiman, ML et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N Engl J Med*. 1996 Feb 1; 334(5):292-5.
- (15) He, J, Kryger, MH, Zorick, FJ, et al. Mortality and apnea index in obstructive sleep apnea: experience in 385 male patients. *Chest* 1988;94(1):9-14
- (16) Engleman, HM, Kingshott, RN, Wraith, PK, et al: Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep Apnea/Hypopnea syndrome. *Am J Respir Crit Care Med* 1999 Feb; 159(2): 461-7
- (17) Faccenda, JF, Mackay, TW, Boon, NA, Douglas, NJ: Randomized placebo-controlled trial of continuous positive airway pressure on blood pressure in the sleep apnea-hypopnea syndrome. *Am J Respir Crit Care Med* 2001 Feb; 163(2): 344-8
- (18) Kaneko, Y, Floras, JS, Usui, K, et al: Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. *N Engl J Med* 2003 Mar 27; 348(13): 1233-41
- (19) Randerath, WJ, Heise, M, Hinz, R et al. An individually adjustable oral appliance vs. continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome. *Chest* 2002 Aug; 122(2):569-75.
- (20) Hubbard, VS and Hall, WH. Gastrointestinal Surgery for Severe Obesity. *Obes Surg* 1991 Sep; 1(3):257-265.
- (21) Sugerman, HJ, Kellum, JM, Engle, KM et al. Gastric bypass for treating severe obesity. *Am J Clin Nutr* 1992 Feb; 55(2 Suppl):560S-566S.
- (22) Rasheid, S, Banasiak, M, Gallagher, SF et al. Gastric bypass is an effective treatment for obstructive sleep apnea in patients with clinically significant obesity. *Obes Surg* 2003 Feb; 13(1):58-61.
- (23) Charuzi, I, Ovnat, A, Peiser, J et al. The effect of surgical weight reduction on sleep quality in obesity-related sleep apnea syndrome. *Surgery* 1985 May; 97(5):535-8.
- (24) Sugerman, HJ, Fairman, RP, Sood, RK et al. Long-term effects of gastric surgery for treating respiratory insufficiency of obesity. *Am J Clin Nutr* 1992 Feb; 55(2 Suppl):597S-601S.

- (25) Ballantyne, GH, Svahn, J, Capella, RF et al. Predictors of prolonged hospital stay following open and laparoscopic gastric bypass for morbid obesity: body mass index, length of surgery, sleep apnea, asthma, and the metabolic syndrome. *Obes Surg* 2004 Sep; 14(8):1042-50.**
- (26) Huerta, DeShields, S, Shpiner, R et al. Safety and efficacy of postoperative continuous positive airway pressure to prevent pulmonary complications after Roux-en-Y gastric bypass. *J Gastrointest Surg* 2002 May-Jun; 6(3):354-8.**
- (27) Nascimento, J, Posner, D, Rogers, M et al. Risks of noninvasive positive pressure ventilation postoperatively in laparoscopic gastric bypass patients. *Crit Care Med* 2006 33(12) A116**