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Mini Review Open Access

The Impact of Obesity and Weight Loss on Patients with Systemic Lupus Erythematosus: Is There a Role for Bariatric Surgery?

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Mini Review

The problem of obesity continues to grow with epidemic proportions in Western countries. Obesity is a complex metabolic disorder characterized by a positive disequilibrium between energy intake and energy expenditure. The consequent expansion of the adipose organ, and in particular of visceral fat depots, increases the risk of developing obesity complications such as insulin resistance, type 2 diabetes, atherosclerosis, steatohepatitis, and cardio- and cerebro-vascular diseases [1].

Individuals with systemic lupus erythematosus (SLE) have an elevated risk of both cardiovascular disease and disability, but the increase in risk for these conditions that may be conferred by obesity is poorly known [2-4].

Weight loss through lifestyle and dietary modification has been shown to improve the clinical manifestations of lupus [5]. However, the effect of bariatric surgery on SLE disease activity and the perioperative morbidity/mortality of weight loss surgery in this population remain to be determined.

Obesity and Systemic Lupus Erythematosus

Among the few studies that have examined obesity in SLE, rates of obesity appear to be higher than in the general population. Katz et al. [6] reported that a large proportion of a community-based sample of women with SLE was obese. Using the most common body composition measure, body mass index (BMI), almost 30% were obese (BMI>30 kg/m^2); using a more sensitive measure, Dual Energy X-ray Absorptiometry (DEXA), half met the criterion for obesity. In such a population they found that the Framingham cardiovascular disease risk score of the obese SLE women was about 80% higher than that of the non-obese group.

A recent study found that among individuals with SLE, 91% experienced disability in at least one valued life activity, and almost half were unable to perform one or more valued life activities. Studies have also reported an increased risk of work disability, and significant impact on the ability to perform activities at home or work [2,3]. This negative impact occurred at a lower BMI than is often considered problematic clinically. Accordingly, some Authors [6] suggest revised cut-points for defining obesity among SLE patients that are substantially lower than those traditionally used (BMI>26.8 kg/m^2 and BMI>30 kg/m^2 respectively).

Most of the reports showed major prevalence of metabolic syndrome (MetS) in lupus patients than in healthy controls. MetS is also common in young patients with recently diagnosed SLE. Moreover, subjects with SLE and MetS presented higher levels of inflammatory markers than SLE without MetS. SLE patients also have a higher risk of experiencing cardiovascular diseases (CVD) and metabolic disorders related to MetS may contribute to overall CVD risk. Moreover, CVD risk is increased when obesity is present in these patients. However, traditional cardiovascular risk factors do not completely explain the enhanced cardiovascular risk in this population. Since the exciting discovery of the secretory properties of adipose tissue, the relationship between obesity and autoimmunity and the understanding of the underlying mechanisms have become of major interest. White adipose tissue is described as an endocrine organ, which secretes a wide variety of factors called adipokines. Adipokines are pleiotropic molecules that contribute to the so-called low-grade inflammatory state of obese subjects creating a cluster of metabolic aberrations including autoimmune and inflammatory diseases that affect joints and bone. In general adipokines are either proinflammatory and diabetogenic (e.g. resistin) or anti-inflammatory and insulinomimetic (e.g. adiponectin), with the former upregulated and the latter downregulated in obesity. Exceptions exist: vistatin has proinflammatory properties but is an insulinomimetic agent. According to the recent literature, all known adipokines are markedly dysregulated when abnormal abdominal fat accumulation is present, thereby promoting metabolic and cardiovascular disorders. Adipokines were recently proposed as novel biomarkers and regulators of MetS, given the association of adipokines plasma concentration and MetS. Thus, MetS and the altered secretion patterns of proinflammatory adipokines present in obesity could be the link between CVDs and rheumatic diseases. Among the different adipokines, leptin and adiponectin were identified as relevant factors involved in interactions between metabolism and rheumatic disorders [7,8].

More recently some Authors have addressed the issue of intestinal microbiota in the aetiopathogenesis of obesity and autoimmune disorders [9]. Our commensal microbiota is a plastic "organ" comprised of trillions of microbes with symbiotic functional capabilities that directly affect human health. Important studies on the relationship of intestinal microbiota with diseases have linked profound changes in the composition of the population and metabolic functions of the gut microbiota to common human intestinal disorders, such as obesity, Crohn's disease and colitis-associated colorectal carcinoma, ulcerative colitis and irritable bowel syndrome, and Clostridium difficile-associated diarrhea. A relevant intestinal dysbiosis was also described in SLE. Recent studies have also suggested that factors, such as antibiotic treatments and diet, and subject characteristics, such as age, may be involved in alterations in the microbiota. Researchers are beginning to recognize and understand the short- and long-term consequences of these changes. Although evidence has suggested an additional link between gut microbiota and

immune disorders, this relationship remains incompletely understood [9].

Surgery and Systemic Lupus Erythematosus

SLE significantly increased the risk of surgical patients for overall major complications and mortality after major surgery [10]. Lin et al. [11] found that surgical patients with SLE had a higher prevalence of preoperative coexisting medical conditions and postoperative major complications. The odd ratio (OR) of 30-day postoperative mortality for surgical patients with SLE was 1.71. Surgical patients who had received more recent (within 6 months) preoperative SLE-related inpatient care had higher risks of 30-day postoperative acute renal failure (OR 7.23), pneumonia (OR 2.60), pulmonary embolism (OR 4.86), septicaemia (OR 3.43), stroke (OR 2.01) than surgical patients without SLE. SLE-related preoperative steroid injections showed a dose-dependent relationship with postoperative complications and mortality.

Patients with SLE are prone to thrombosis especially if they have history of vascular thrombosis, heart failure, pulmonary hypertension, or if they are positive for anti-phospholipid antibodies (APA) and/or lupus anticoagulant (LAC). On the other hand, lupus patients with positive APA and/or LAC, hypersplenism, anti-platelet antibodies and blood marrow suppression due to SLE per se or immunosuppressant may present with severe thrombocytopenia which may complicate invasive procedures due to an excessive bleeding risk.

Moreover perioperatively, SLE can present major challenges to the anesthesiologist because of accrued organ damage, coagulation defects, and complex management regimes [12].

Bariatric Surgery, Morbid Obesity and Systemic Lupus Erythematosus

For the morbidly obese (BMI >40 kg/m^2), bariatric surgery has been the most durable treatment. Bariatric surgical procedures modify the anatomy of the gastrointestinal tract and thereby reduce caloric intake or absorption.

Restrictive procedures include adjustable gastric banding (wrapping a silicone inflatable band around the stomach to create a small pouch with a narrow outlet), and sleeve gastrectomy. Adjustable gastric banding includes the insertion of a subcutaneous reservoir so that gastric restriction can be adjusted by means of saline injections. Another recently developed restrictive procedure is the vertical (sleeve) gastrectomy, in which resection of much of the gastric body leaves a narrow tube of stomach as an alimentary conduit.

Proximal Roux en Y gastric bypass is often referred to as a combination restriction-malabsorption procedure. It involves stapling of the stomach to create a small (≤ 30.0 ml) upper gastric pouch. The small intestine is then divided at the midjejunum, and the distal portion (called the alimentary, or Roux, limb) is anastomosed to the gastric pouch. The distal portion of the stomach and proximal small intestine (the bilio pancreatic limb) are anastomosed end to side farther down the jejunum. Food comes into contact with pancreatic and biliary secretions only below this anastomosis, in the segment of small intestine called the common channel. The shorter the common channel (and the longer the Roux limb), the less nutrient absorption will occur.

Malabsorptive procedures that introduce less gastric restriction than the Roux enY procedure include biliopancreatic diversion, commonly done by means of a procedure called duodenal switch, which includes sleeve (vertical) gastrectomy. Some surgeons perform a sleeve gastrectomy as the initial part of a staged operation, performing a Roux en Y procedure after initial weight loss has made surgery less difficult and reduced the operative risk [13].

In the United States gastric bypass operations account for about 70% of procedures, laparoscopic gastric banding about 25%, and sleeve gastrectomy, duodenal switch, and other procedures about 5% [14].

Weight loss has been shown to have clinical benefits in patients with lupus. A dietary intervention study of stable SLE patients on low dose prednisone suggests significant weight loss over a 6 week period can achieve clinical improvement [5]. However, failure to adhere to long-term diet regiments and difficulty maintaining weight loss (especially in those with mobility issues) are potential pitfalls to this approach and suggest a potential role for bariatric surgery in morbidly obese lupus patients.

There is little published on the outcomes of bariatric surgery in SLE patients. In a retrospective study of the effect of immunosuppressive therapy on 61 patients undergoing bariatric surgery, which included a wide variety of diseases (asthma, endocrine deficiency, autoimmune disorders) and the outcomes of only 4 lupus patients, the early complication rate (30 day) was 16.3% [15].

Recently I had the pleasure to review and comment a paper by Corcelles et al [16,17] that has been accepted for publication in SOARD (Surgery for Obesity And Related Diseases), reporting on 31 morbidly obese patients with SLE who underwent bariatric surgery between 2005 and 2013 at the Cleveland Clinic in Ohio (USA). Twenty-three subjects had laparoscopic Roux-en-Y gastric bypass, 3 underwent laparoscopic revisional surgery for failed bariatric procedure, 3 had laparoscopic sleeve gastrectomy and one underwent laparoscopic adjustable gastric banding. Mean age, BMI and excess weight at baseline were 52.8 ± 9.4 years, 44.3 ± 9 kg/m^2 and 52.5 ± 25.7 kg, respectively. Of these 31 patients, 24 (77.4%) were taking immunosuppressive medications at the time of surgery. Early major postoperative complications occurred in 4 patients (12.9%), with 3 requiring reoperation (9.6%). Multivariate analysis identified immunosuppressive therapy to be significantly associated with postoperative complications (p=0.05). At a mean follow-up of 3 years, 13 patients (42%) showed reduction in the number of immunosuppressive medications and 6 (19.3%) were off steroids completely. After bariatric surgery, mean BMI decreased to 34.2 ± 8.2 kg/m^2 (p<0.005) and percentage excess weight loss was 51.2 ± 33.4%.

Silicone Implantation and Systemic Lupus Erythematosus

Some concerns arise from the utilization of silicone gastric banding in SLE morbidly obese patients. In fact although the association between silicone and connective tissue diseases has been thoroughly refuted via meta-analysis, there still remain numerous case reports of the development of connective tissue disease after procedures that involve the use of silicone [18]. Some experimental studies suggest that silicone implantation may influence immunological response during murine lupus, including the provocation or exacerbation of autoantibodies. Objective data have demonstrated that patients with immune-mediated reactions to silicone implants had increased IgG in surrounding tissue when compared with asymptomatic implanted patients. In addition, serum anti-silicone antibodies have been more frequently detected in patients with silicone implants when compared

with controls. Although speculative, it seems plausible that a subgroup of silicone implanted patients may be at risk of developing autoimmune diseases [19-22].

In recent years, four conditions, among which siliconosis, were linked to a previous exposure to an adjuvant, and it has been described a syndrome entitled Autoimmune/inflammatory Syndrome Induced by Adjuvants (ASIA) [23-25].

In conclusion bariatric surgery appears to be an option in SLE morbidly obese patients, however laparoscopic silicone gastric banding should be prudentially avoided. Even if weight loss after bariatric surgery could be associated with decreased immunosuppressive therapy requirements, the risk is higher than average and bariatric surgery in this patient population should be approached with caution.

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