

A Narrative Review Study on the Effects of Obesity and Bariatric Surgery on Multiple Sclerosis

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Abstract

Obesity is a major public health concern and should be considered in autoimmune inflammatory disorders, such as multiple sclerosis (MS). In these patients, obesity leads to increasing comorbidities as well as reduced quality of life. Obesity causes an inflammatory state in the body, especially in adolescents; obesity has a role in the pathogenesis of MS. Hence, it is identified as a lifestyle modifiable risk factor for MS disease. Among various treatments for obesity, bariatric surgery has been widely used. Although few studies have been performed on bariatric surgery in MS patients, in this review, we present the existing data regarding the effects of obesity on the MS course and evaluate the outcomes of bariatric surgery among this population.

Keywords: Bariatric surgery, multiple sclerosis, obesity

CONTEXT

The prevalence of obesity is increasing worldwide, and it is a major public health concern.^[1,2] Obesity is a risk factor for many metabolic and nonmetabolic disorders.^[3] A disorder that is affected by obesity is multiple sclerosis (MS), an autoimmune inflammatory disease of the central nervous system (CNS).^[1,3] Obesity in MS patients can lead to increased cardiovascular comorbidities and reduced quality of life.^[3,4] Therefore, attention to weight control and maintaining a normal body mass index (BMI) need to be looked at in addition to mainstream treatment in MS.

Over time, one of the advancements in the treatment of obesity has been surgical interventions. The basis for this procedure, which is used to treat severe obesity (BMI ≥ 35), is to limit calorie intake and reduce food absorption from the gastrointestinal (GI) tract.^[4] As a result of rapid and significant weight loss, it puts a person at risk of complications.^[4] Although bariatric surgery is safe and effective, the outcomes of studies with respect to this procedure in MS patients are limited.

In this review, we evaluated the outcomes of bariatric surgery as well as its safety and efficacy among MS patients, and the other aim is to determine if bariatric surgery is recommended to treat obesity among MS patients.

Data collection

The search was conducted using the terms “obesity,” “multiple sclerosis,” and “bariatric surgery” in PubMed and Google Scholar databases. In this study, English language papers on the effect of obesity and bariatric surgery on MS published in 2012–2020 were considered.

Obesity and its effects on MS

Several modifiable risk factors have been identified in the development of MS and its progression, including smoking, alcohol consumption, cardiovascular disorders, infectious mononucleosis, low level of vitamin D, and, most recently, obesity.^[2,5] Various studies have implicated the possible role of obesity, especially during adolescence in the pathogenesis of MS.^[2] The pathophysiologic mechanisms of this condition include an increase in the level of pro-inflammatory cytokines such as leptin and a decrease in the bioavailability of vitamin D as a result of its sequestration in fat tissues.^[6,7] In fact, obesity can cause a low-grade inflammatory state in the body.^[6] This is done through activation of T helper 1 lymphocytes, CD8 T cells, and B lymphocytes, which eventually lead to the secretion of leptin, interleukin 1 and 6, TNF α , and various inflammatory mediators.^[3] Leptin also increases the proliferation of autoreactive T cells and inhibits the proliferation of T regulatory cells.^[8] Therefore, it seems a healthy lifestyle profile

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Submitted: 17-Mar-2021 **Revised:** 15-Apr-2021 **Accepted:** 17-Jul-2021

Published: 14-Oct-2021

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DOI: 10.4103/aian.AIAN_235_21

switches the basic pathogenesis of MS from pro-inflammatory to anti-inflammatory state.

A prospective study by Bistrom *et al.* showed that a rise in leptin level was associated with an increased risk of MS in people younger than 20 years of age. In fact, serum leptin level directly correlated with BMI and revealed a clear difference between both genders (about five times higher among females).^[9]

A 5-year study investigating the effects of obesity on the progression of MS found that BMI ≥ 30 can be a predictor for at least a one-point increase in expanded disability status scale (EDSS) among patients with mild disability (EDSS ≤ 4). In addition, this study showed that there was a significant difference between baseline BMI and brain MRI changes (new T2 lesions and/or Gd enhancing lesions) during these 5 years. On the contrary, brain MRI changes were higher among obese and overweight patients in comparison to patients with normal BMI. However, in this study, there was no association between BMI and MS relapses within one year of the study.^[10] This was in contrast to the results of a study by Rachel Galisto on 3046 patients with MS that revealed no significant association between BMI and brain MRI outcomes.^[11]

Stampanoni *et al.*^[12] in a study on 140 patients with MS found a significant relationship between BMI and EDSS, stating that a high BMI was associated with increased disability in relapsing remitting MS patients. In addition, this study showed that high BMI was linked to a high level of pro-inflammatory cytokines, such as leptin and interleukin 6 (IL6) as well as a reduced level of anti-inflammatory cytokine (interleukin 13) in cerebrospinal fluid (CSF). Increased pro-inflammatory cytokines in CSF accelerates disease reactivation and neurodegeneration in MS. They concluded that obesity is associated with disability worsening in MS. According to their findings, a significant relation between dyslipidemia (increased triglyceride (TG) and TG/HDL ratio) and the level of IL6 in CSF was present.^[12]

Another study by Manouchehrinia *et al.*^[13] showed that high BMI was associated with an increased risk of conversion to secondary progressive MS.

In a cross-sectional study on more than 5000 MS patients, Fitzgerald *et al.* found that increased abdominal fat is associated with severe disability and progression in MS. It is believed that abdominal adipose tissue produces pro-inflammatory cytokines, which in turn increases inflammation and oxidative stress in the brain. In contrast, this study showed that total adiposity (as measured by BMI) is not a strong predictor of disability in MS. However, it was not clear whether an increase in waist circumference led to further disability or obesity had occurred as a result of increased disability.^[14]

Finally, obesity is recognized as a risk factor for severe COVID-19 infection and its mortality as well as morbidity in the MS population.^[15]

Bariatric surgery and its neurologic complications

With the ever-increasing prevalence of obesity and limited efficacy of medical treatment, surgical strategies are considered for the treatment of morbid obesity (BMI ≥ 35 or BMI ≥ 40) and obesity-related comorbidities.^[7,16] The basis for most procedures are often laparoscopically,^[17] which is to achieve significant and sustainable weight loss by limiting calorie intake and/or reducing food absorption from the gastrointestinal tract.^[7,17]

Generally, four surgical procedures are used to treat obesity with various degrees of effectiveness as well as adverse effects: gastric binding, sleeve gastrectomy, gastric bypass Roux-en-Y, and biliary pancreatic shunt.^[17,18] Based on the International Federation for the Surgery of Obesity, sleeve gastrectomy and Roux-en-Y are utilized more than the other procedures.^[16]

According to studies, neurologic complications following bariatric surgery are estimated to be between 5% and 15%^[18] and have been mainly due to numerous nutritional deficiencies such as the lack of water and fat-soluble vitamins and various minerals deficiencies.^[17] If these deficiencies are not diagnosed and treated in time, they can lead to irreversible consequences on the nervous, musculoskeletal, and other body organs.^[7]

In a study conducted in the Middle East on the neurologic complications of bariatric surgery, 3% of patients had neurologic complications following bariatric surgery, which included peripheral neuropathy, vitamin B12, and copper deficiency, and one case of Wernicke encephalopathy. In this study, all the patients with neurologic complications recovered, except one patient with Guillain Barre Syndrome, who eventually died of a massive pulmonary embolism. Moreover, improvement in obesity-related comorbidities following bariatric surgery was observed, such as better control of diabetes and blood pressure, improvement in primary intracranial hypertension, and obstructive sleep apnea.^[18]

In a case series of three patients who underwent bariatric surgery, all had neuropathic symptoms post operation, which is confirmed by nerve conduction studies. Two patients with Wernicke encephalopathy and one patient with myelopathy due to vitamin B12 deficiency were reported. Two patients developed Parkinsonism following surgery (one patient after several weeks and the other 6 years after surgery); although the etiology of Parkinsonism following bariatric surgery is not known, vitamin D deficiency might play a role. All the patients in this study experienced intractable vomiting before the onset of the symptoms.^[19]

In another study, 26 cases with neurological consequence after bariatric surgery were reported. The most common complication among these patients was axonal polyneuropathy. Five patients had CNS demyelination, which was clinically presented by MS relapse or MS-like attacks. However, optic neuritis, myelitis, acute brachial neuropathy, and three cases of motor neuron disease were reported.^[20]

The time interval between performing bariatric surgery and the occurrence of neurologic complications is highly variable.

Neurologic problems can occur immediately after surgery (for example, compression neuropathies and meralgia paresthetica) or in the long term.^[18] Nonetheless, neurologic outcomes after bariatric surgery vary and depend on the severity and duration of malnutrition.^[19]

Bariatric surgery and MS

Bariatric surgery has a limited role in the management of obesity itself. Few studies have evaluated the true safety and efficacy of obesity surgical treatment and the outcomes of bariatric surgery among the MS population, but there has not been much basic research showing bariatric surgery causes a shift toward good immunity/immune tolerance. The first case-control study was performed by Kalman Bencsath *et al.* in 2004–2012. In this study, a good safety profile of bariatric surgery was shown among MS patients and any cases of disease worsening or increased relapse rate following surgery were not observed. In addition, patients who underwent bariatric surgery exhibited improvement in walking ability (evaluated with time 25-foot walk “T25FW”) due to weight loss. In addition, the use of disease-modifying therapies for MS did not exert any adverse effect on the surgical outcomes.^[21]

In the study conducted by Sean Burn *et al.*^[22], out of the eight patients who underwent bariatric surgery, two reported exacerbation of MS symptoms post operation, but there was no rapid progression of the disease during follow-up. This study confirmed the relative safety and efficacy of bariatric surgery in MS patients and showed that bariatric surgery can reduce comorbidities, leading to better control of diabetes and hypertension among patients with MS. Nevertheless, few cases of CNS demyelinating syndrome were reported after this surgery.

Generally, severe and rapid weight loss is always associated with the risk of nutritional deficiency and release of inflammatory cytokines. Dr. Moghadasi *et al.* reported four cases of definite MS after severe weight loss following nonsurgical dietary treatment.^[23] Similarly, Foziah Alshamrani *et al.*^[24] reported five cases with new-onset MS following bariatric surgery, but no direct link was found between their surgery and occurrence of MS. Nonetheless, it is likely that nutritional deficiency, especially vitamin D deficiency, which is a known risk factor for MS, played a role in this issue.

In addition, bariatric surgery by altering the anatomy and physiology of the GI tract can affect the intake, digestion, and absorption of proteins;^[25] this can put the patient with MS at risk. Studies on the effects of protein malnutrition after bariatric surgery in patients with MS are far too few; Sorgun *et al.* showed that low serum albumin level was independent of the disease course, number of attacks, and EDSS.^[26] However, more studies are warranted in this area. A minimal daily protein intake of 60 g is recommended to prevent protein malnutrition and its complications after bariatric surgery.^[25]

Finally, obesity among patients with MS is associated with a higher rate of depression and fatigue and less mobility; this risk

is subject to change following bariatric surgery. Carolyn Fisher showed that patients with MS who underwent bariatric surgery were affected by different range of depressive symptoms than obese patients with MS who were not treated. Depressive symptoms in these patients decreased during the first year after surgery and then increased over time.^[4] Therefore, careful psychological evaluation is imperative before and after the surgery.

CONCLUSION

Obesity, especially visceral obesity, is associated with various metabolic and immune-inflammatory disorders. Obesity causes imbalance of various inflammatory and anti-inflammatory factors and interferes with vitamin D metabolism. These changes are associated with the development of MS and/or its progression. Findings from different studies show a direct causal link between obesity and MS progression and worsening disability. Therefore, treatment of obesity and maintaining a normal BMI to be one of the priorities in MS.

Bariatric surgery has been used as an effective method to treat morbid obesity and obesity-related comorbidities. Despite the relative safety and efficacy of bariatric surgery among MS patients, it should be stated that severe and rapid weight loss by inducing nutritional deficiencies and sometimes with protein-calorie malnutrition can complicate the MS status. Nonetheless, information on the outcomes of bariatric surgery among patients with MS is limited and careful monitoring of these patients who want to undergo surgery is recommended to monitor the nutritional status pre- and post-surgery.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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