



The Impact of ADHD on Outcomes Following Bariatric Surgery: a Systematic Review and Meta-analysis

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Abstract

The objective our study was to carry out a systematic review and meta-analysis to examine the impact of attention-deficit and hyperactivity disorder (ADHD) on bariatric surgery outcomes. Despite the effectiveness of bariatric surgery, about 10 to 20% of patients continue to regain weight after the procedure. New evidence supports that ADHD may be directly associated with obesity and may affect outcomes following bariatric surgery. However, certain psychiatric illnesses, such as ADHD, are rarely screened for, leading to a continued lack of data on the interaction between ADHD and bariatric surgery. A comprehensive literature search for both published and unpublished studies of ADHD and bariatric surgery from 1946 to August 2018 was performed. The search was conducted using the Medline, EMBASE, Scopus, the Cochrane Library, and Web of Science databases as well as conference abstracts. Our search strategy terms included “(ADHD OR attention deficit hyperactivity disorder) AND (bariatrics OR obesity surgery OR gastric bypass OR gastric sleeve OR Roux-en-Y OR RYGB OR sleeve gastrectomy)” and was limited to human studies in the English language. Preliminary database search of the literature yielded 104 articles after 70 duplicates were removed. A total of five studies with 492 patients were included. The overall ADHD rate was 20.9% with reported rates ranging from 7 to 38%. The weighted mean age was 44.0 ± 10.2 years, the weighted sex was 83.6% female, and the weighted mean follow-up was 22.2 months. Preoperative weighted mean BMI was 43.7 versus a postoperative weighted mean BMI of 34.7. No statistical significance was observed for mean BMI difference between non-ADHD vs. ADHD patients undergoing bariatric surgery (three studies; MD -2.66 ; CI -7.54 to 2.13 ; $p=0.28$). Statistical significance was, however, observed for postoperative follow-up between patients with ADHD vs. non-ADHD subjects (three studies; MD -7.28 ; -13.83 to -0.73 ; $p=0.03$). Patients with ADHD do not have a statistically significant mean BMI difference following bariatric surgery but have a statistically significant reduction in postoperative follow-up versus non-ADHD patients. Targeted strategies aimed at improving clinic attendance for this at-risk ADHD population may improve bariatric outcomes and minimize recidivism rates.

Keywords Obesity · Obesity surgery · ADHD and obesity · ADHD and bariatric surgery

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Introduction

Despite the effectiveness of bariatric surgery, approximately 10 to 20% of patients continue to experience weight recidivism [1–4]. Multiple factors are responsible for weight recidivism and potential failure of surgery. Among those factors are mental health disorders such as anxiety, depression, eating disorders, and attention-deficit and hyperactivity disorder (ADHD) [4–6]. New evidence supports that psychiatric disorders may be directly associated with obesity and that their core symptoms improve following weight loss [7–9]. Research also suggests that patients with psychiatric illnesses severely affecting cognitive and functional status have difficulty complying with medications, diet and exercise regimens, and follow-up visits after bariatric surgery [10]. As a result, this population is associated with poorer outcomes following surgery [9].

ADHD is an inherited neurological disorder present in approximately 5% of the adult population [11, 12]. Diagnosis is based on the following traits using the DSM-IV criteria: distractibility, impulsiveness, and inattention. Treatment of ADHD is primarily pharmacologic, with amphetamine stimulants providing good efficacy with minimal side effects. Studies on the molecular biology and underlying causes of ADHD are ongoing, though its neurophysiologic mechanism is thought to be shared with that of eating disorders and obesity [10, 12–14]. There is evidence of increased ADHD prevalence among those with obesity, leading to greater difficulty in adherence to treatments and weight control. However, few studies have evaluated the prevalence of ADHD in candidates for bariatric surgery and no study has evaluated its possible effects on outcomes following surgery [15, 16].

Recent research has identified an association between obesity and ADHD. Rates of ADHD were found to be sixfold greater (27.4%) in adults seeking treatment for obesity versus the general population [17–20]. These rates further increased to 42.6% among those with a body mass index (BMI) over 40. This association between mental health and obesity has made it standard of care to assess for the presence of eating disorders and major depressive disorder before bariatric surgery [16, 21]. Despite this, certain psychiatric illnesses such as ADHD are rarely screened for, leading to a continued lack of data on the prevalence and impact of ADHD in bariatric surgery patients.

The objective of our study was to carry out a systematic review and meta-analysis on the impact of ADHD on bariatric surgery outcomes. The primary outcome of interest included mean BMI change between ADHD versus non-ADHD patients. Secondary outcomes include follow-up, ADHD core symptom reporting, and substance abuse.

Materials and Methods

Search Strategy

A comprehensive literature search for both published and unpublished studies of ADHD and bariatric surgery from 1946 to August 2018 was performed. The search was conducted using the Medline, EMBASE, Scopus, the Cochrane Library, and Web of Science databases, as well as conference abstracts. Our search strategy terms included “(ADHD OR attention deficit hyperactivity disorder) AND (bariatrics OR obesity surgery OR gastric bypass OR gastric sleeve OR Roux-en-Y OR RYGB OR sleeve gastrectomy)” and was limited to human studies in the English language. Additional manual searches of reference lists were performed to identify potentially missed articles. Gray literature was also identified using Google.

Selection Criteria

Abstracts and titles were first screened for inclusion by two independent reviewers (VM and IT). Irrelevant papers based on their title and abstract were not included for full-text evaluation. Abstracts were screened based on the following inclusion criteria: adult patients (age ≥ 18 years old), studies with > 5 subjects, and studies where both ADHD and non-ADHD patients underwent bariatric surgery. All ADHD was defined using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Discrepancies were resolved by consensus or through assessment by a third independent reviewer (JD). Exclusion criteria included non-English studies, duplicate studies, kin studies, or studies with an incorrect comparator. Full-text articles of all selected abstracts were further reviewed by two reviewers (VM and IT) using the same criteria and disputes were resolved by a third reviewer (JD). Included studies were then assessed for methodological quality and bias using the MINORS tool for non-randomized trials [22].

Data Extraction

Pertinent data was collected from selected trials by one reviewer (VM) and a second reviewer checked for accuracy (IT). The primary outcome of interest included the mean BMI change for ADHD vs. non-ADHD patients. Secondary outcomes included follow-up, quality of life, reported mental health improvement, and substance abuse. The following patient characteristics were assessed: age, sex, pre- and postoperative BMI, and pre- and postoperative ADHD self-reported symptom scoring.

Statistical Analysis

Categorical variables were reported as frequencies and percentages, and continuous data was expressed as mean \pm standard deviation. Meta-analysis was conducted where possible for bariatric surgery patients with and without ADHD. Outcomes assessed in the meta-analysis included mean BMI change and mean follow-up. The estimated effects were calculated using Revman 5.3 software obtained from the Cochrane website [23]. Included studies were then tested for heterogeneity using the chi-square test with significance set at $p < 0.10$ and the amount of heterogeneity was quantified by the I^2 statistic as follows: (1) low $> 25\%$, (2) moderate $> 50\%$, and (3) high $> 75\%$ [24].

Results

Study Selection

Preliminary database search of the literature yielded 104 articles after 70 duplicates were removed (Fig. 1). After initial

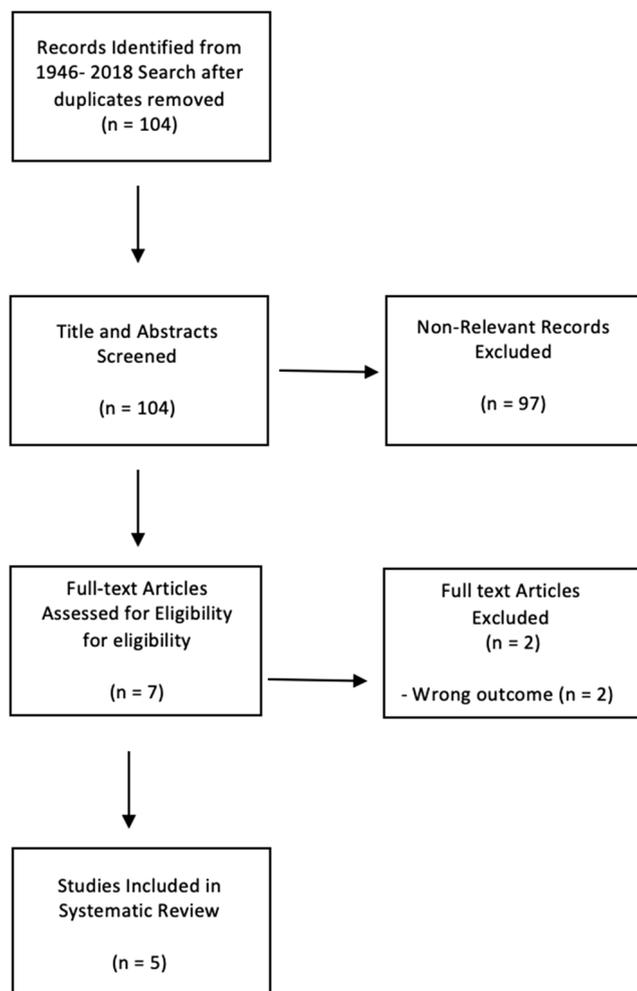


Fig. 1 PRISMA diagram with search results for systematic review

screening of titles and abstracts, seven studies underwent full-text assessment for eligibility. Five manuscripts met inclusion criteria and were included in the final systematic review. Included manuscripts consisted of four cohort studies and one case-control study.

Basic Demographics

A total of five studies [8, 17, 19, 20, 25] with 492 patients were included (Table 1). The overall ADHD rate was 20.9% with reported rates ranging from 7 to 38%. The weighted mean age was 44.0 ± 10.2 years, the weighted sex was 83.6% female, and the weighted mean follow-up was 22.2 months. Preoperative weighted mean BMI was 43.7 kg/m^2 versus a postoperative weighted mean BMI of 34.7 kg/m^2 . There was no statistical significance between baseline variables of reported studies; however, subgroup analysis for several studies revealed a trend towards statistical significance for the presence of ADHD and a higher BMI.

Quality Assessment of Included Studies

Studies were assessed for bias and methodological quality using the MINORS criteria (Table 2). No study met the global ideal score for comparative studies, limited in prospective calculation of ideal study size and loss to follow-up greater than 5%.

Outcomes

Mean BMI Change

No statistical significance was observed for mean BMI change between non-ADHD vs. ADHD patients undergoing bariatric surgery (Fig. 2) (three studies [17, 20, 25]; MD -2.66 ; 95% CI -7.54 to 2.13 ; $p = 0.28$). Heterogeneity was high and statistically significant ($p = 0.002$; $I^2 = 84\%$).

Follow-up

Statistical significance was observed for postoperative follow-up between patients with ADHD vs. non-ADHD subjects (Fig. 3) (three studies [17, 20, 25]; MD -7.28 ; 95% CI -13.83 to -0.73 ; $p = 0.03$). Heterogeneity was low and not statistically significant ($p = 0.67$; $I^2 = 0\%$).

ADHD Symptom Improvement and Substance Abuse

Two studies reported on the perceived change in ADHD symptoms following bariatric surgery. Alfonsso et al. revealed an improvement in ADHD symptoms for patients undergoing bariatric surgery using the ADHD Self Rating Scale (ASRS). In contrast, Nicolau et al. demonstrated no difference

Table 1 Basic demographics of included studies

	Study design	Total patients (n)	Female (%)	Diagnosis of ADHD	ADHD scoring	Groups	Follow-up (month)	Patients (n)	Mean age (year)	Preop BMI (kg/m ²)	Postop BMI (kg/m ²)
Alfonsson 2014	Cohort	129	78	–	ASRS	ADHD	12	–	42.8	–	–
Nicolau 2015	Case control	60	78	DSM-IV	ASRS	No ADHD	–	–	–	–	–
Altfas 2002	Retrospective cohort	215	78	DSM-IV	–	ADHD	51	19	46.4	45.9	32.2
Marchesi 2017	Prospective cohort	40	93	DSM-IV	ASRS	No ADHD	44.4	41	46	49.5	34.5
Steinmann 2011	Cohort	120	83	DSM-IV	–	ADHD	38.7	59	–	39.2	36.6
						No ADHD	28.6	84	43	34.6	30.6
						ADHD	12	15	48.3	47.1	32.5
						No ADHD	–	25	–	42	28.5
						ADHD	12	–	42.9	50	31.9
						No ADHD	–	–	–	–	–

DSM diagnostic and statistical manual, ASRS adult ADHD self-reporting scale

in quality of life, ADHD, or depressive symptoms postoperatively using the ASRS and Beck Depression Inventory scales. Both studies were able to demonstrate an association between elevated alcohol consumption and patients with continuing ADHD symptoms following surgery.

Discussion

This is the first systematic review and meta-analysis addressing the role of ADHD in patients undergoing bariatric surgery. We identified a total of five studies with 492 patients. The overall ADHD rate was 20.9%, in keeping with prior literature. Results of our meta-analysis revealed that patients with ADHD did not have a statistically significant mean BMI change following bariatric surgery in comparison to their non-ADHD counterparts. ADHD patients, however, did have statistically lower rates of postoperative follow-up, with a mean follow-up difference of 7.3 months versus non-ADHD patients.

The pathophysiology of ADHD and its close association with obesity is complex and relies upon intricate neurophysiological mechanisms [17]. Attention has recently been drawn to genetic dopamine receptor (DR) dysfunction as a basis for both ADHD and obesity [26]. Deficiencies in the DRD2 dopamine gene are associated with *reward deficiency syndrome* leading to a decrease in total dopamine levels. Lowered dopamine levels are thought to predispose individuals to seek unnatural reward mechanisms such as gambling, binge eating, and substance abuse [13, 14, 17, 26]. Such mechanisms predispose patients to weight gain, which in turn has further been demonstrated to perpetuate DR dysfunction. This feedback cycle is just one mechanism associated with the progression of obesity, and why future studies are needed to address the neurobiology of obesity and mental health disorders.

Previous literature has examined the impact of ADHD on bariatric outcomes. Levy et al. conducted a case-control study of 78 subjects with ADHD and severe refractory obesity [27]. Preoperative amphetamine pharmacologic treatment of ADHD was associated with sustained long-term weight loss. This was attributed to reduced binge eating and impulsivity due to reported improvements in anxiety, time management, and self-awareness. These pharmacologic benefits were specific solely to ADHD patients with obesity, as amphetamine trials for patients with obesity alone have been plagued by high attrition, minimal efficacy, and significant side effects. In addition, Nielsen et al. performed a cross-sectional study of 248 pre- and postbariatric surgery patients with ADHD [9]. They observed no correlation between ADHD and weight loss postoperatively but did identify improvement in core ADHD symptoms following surgery. These studies, however, were limited by selection bias, study design, and non-generalizable comparators.

Table 2 MINORS assessment of included studies

Criteria	Study				
	Alfonsson 2014	Nicolau 2015	Altfas 2002	Marchesi 2017	Steinmann 2011
A clearly stated aim	2	2	2	2	2
Inclusion of consecutive patients	2	2	1	2	1
Prospective collection of data	1	2	1	2	2
Endpoints appropriate to the aim of the study	2	2	2	2	1
Unbiased assessment of the study endpoint	2	2	2	2	2
Follow-up period appropriate to the aim of the study	2	2	2	2	2
Loss to follow-up less than 5%	2	1	0	2	1
Prospective calculation of the study size	0	0	0	0	0
An adequate control group	2	2	2	2	2
Contemporary groups	2	2	2	2	2
Baseline equivalence of groups	2	2	2	2	1
Adequate statistical analyses	2	2	2	2	2
Total*	21	21	18	22	18

† The items are scored 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). The global ideal score being 16 for non-comparative studies and 24 for comparative studies

Our study is novel in several ways. To the best of our knowledge, this represents the first systematic review and meta-analysis on the impact of ADHD and weight loss following bariatric surgery. We identified a global improvement in subjective core ADHD symptoms following surgery, but also a potential increased risk for alcohol abuse. These patients therefore warrant structured multidisciplinary follow-up with mental health practitioners to identify and support those at risk for developing substance abuse. Our analysis also revealed statistically lower rates of follow-up for ADHD patients. Weight recidivism correlates highly with inability to reliably attend an often-demanding bariatric clinic schedule. Targeted strategies aimed at improving clinic attendance for at-risk ADHD populations may improve outcomes and minimize recidivism rates.

This study is not without limitations. Although a comprehensive search has been conducted, the literature surrounding this topic is not robust, affecting our ability to identify more complex interactions between ADHD and bariatric surgery. We were only able to identify five studies, limiting our study’s generalizability. Furthermore, no included study achieved a global ideal bias score using the MINORS tool. Both selection and recall bias were present due to retrospective nature of data

and use of self-reported survey assessments. Importantly, of included studies, no details were provided regarding which, if any, patients underwent concurrent pharmacologic ADHD treatment. Amphetamine therapy is a significant potential confounder given its previously described efficacy for sustained long-term weight loss following bariatric surgery and improvement in executive function. It is possible that delaying surgery in the ADHD population until symptoms are controlled pharmacologically would result in the lack of postoperative differences observed in BMI between groups. Bariatric clinics and surgeons may also create a selection bias by selecting operative patients with well-controlled or treated ADHD. Overall mean weighted follow-up for our studies was 22 months, which may not be a sufficient time interval to adequately compare weight recidivism between groups. There may also be a difference between self-reported and objective neuropsychological impairment obtained by using the ADHD Self Rating Scale. The sensitivity and specificity for the ASRS are 77% and 76% respectively which may lead to a number of false positives, particularly given the higher rates of depressive and anxiety symptoms in the bariatric cohorts [17]. However, the studies included in the meta-analysis attempted to account for such confounders. Marchesi et al.

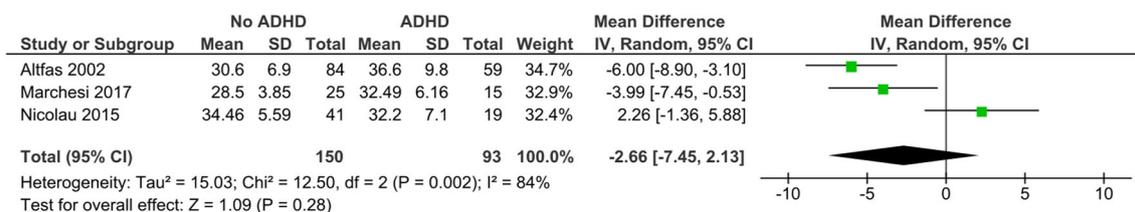


Fig. 2 Mean BMI change for non-ADHD vs. ADHD bariatric surgery patients

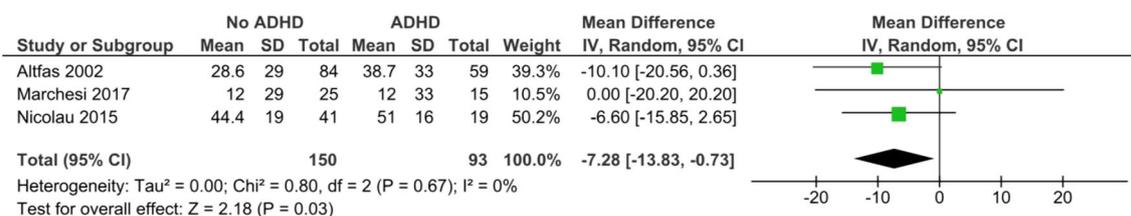


Fig. 3 Mean follow-up difference for non-ADHD vs. ADHD bariatric surgery patients

excluded patients with depression, or those receiving psychoactive medications. Altfas et al. only included patients with stable anxiety or depression as to not obscure an ADHD diagnosis. While Nicolau et al. did include patients with depression and anxiety, they administered concurrent depression and anxiety surveys to both ADHD and non-ADHD study groups. No difference in depression was found between groups based on self-reporting. Despite these issues, the present study is the most comprehensive analysis of ADHD and its outcomes following bariatric surgery.

In addition, individuals with ADHD are known to have elevated risks of other concomitant mental health disorders, yet only one article by Steinman et al. reflected these rates. This relationship is important as recent studies have demonstrated that poor preoperative cognitive status is closely associated with adverse prolonged weight loss [28, 29]. It is possible that some patients may also possess cognitive dysfunction with respect to measures commonly impaired with ADHD such as executive function and learning. Disparity in findings between these two groups may exist because patients with ADHD are most commonly diagnosed in childhood when appropriate medical and behavioral intervention is started. This early diagnosis and intervention may be why up to 60% of individuals with ADHD experience partial remission of symptoms and improvement in cognitive function upon entering adulthood [9]. In contrast, patients without an ADHD diagnosis, but otherwise reduced cognitive performance may be less likely to respond to the same therapy or undergo similar disease regression.

ADHD phenotypes are diverse and include inattentive, hyperactive-impulsive, or a combination of types. Such details are not always captured by surgical literature and may potentially affect weight loss following bariatric surgery. Overall, mental illnesses convey a spectrum of disease and thus may affect an individual's function in a number of ways in which our study was not designed to capture. The strength of our study, however, was that all individuals were followed and pre-screened in well-established bariatric clinics. As a standard of care, bariatric surgery would only be offered in patients with controlled mental health disease, able to appreciate the risks and benefits of surgery, and demonstrate an ability to partake in appropriate follow-up.

In conclusion, this study demonstrates no association between ADHD and adverse weight loss outcomes in patients

undergoing bariatric surgery; however, ADHD patients display decreased follow-up postoperatively. A paucity of literature surrounding the complex interaction between ADHD and obesity exists. Future studies are needed to help clarify the neurophysiologic mechanisms of obesity and their impact on associated mental health disorders.

Conclusion

Compared to patients without ADHD, patients with ADHD do not have a statistically different mean BMI change. However, they were found to have lower rates of postoperative follow-up on meta-analysis. Targeted strategies aimed at improving postoperative clinic attendance for ADHD populations may improve bariatric outcomes and minimize weight recidivism.

Compliance with Ethical Standards

Conflict of Interest Authors 1, 2, 3, and 4: none to declare

Author 5 is a consultant and has received educational grants from Ethicon and Covidien, educational grants from Stryker, and teaching honoraria from Cook Surgery and Bard Davol.

Author 6 is a consultant for Gore Medical and Ethicon.

Ethical Approval and Consent This article does not contain any studies with human participants or animals performed by any of the authors.

For this type of study, formal consent is not required. Informed consent does not apply.

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