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Obesity surgery among people with schizophrenia or bipolar disorder:

A systematic review of outcomes and recommendations for future research

Background:

People with schizophrenia or bipolar disorder (BD) exhibit very high levels of obesity. Little is known about the potential benefits/risks of obesity surgery. We conducted a narrative review to summarize the available knowledge on bariatric surgery in people with schizophrenia or BD.

Methods:

A systematic search was conducted of major electronic databases from inception to October 2016 for studies investigating bariatric surgery among people with schizophrenia or BD. Data were presented in a narrative synthesis and future research strategies proposed.

Results:

The electronic database searches identified 44 records. Eight studies (BD, n=265; Schizophrenia: n=14) were included with a mean study length of 15.7 months (12-24). Seven found that bariatric surgery resulted in weight loss in those with psychiatric disorders with an excess weight loss ranging -31% to -70%. Six studies found that weight loss from bariatric surgery was similar in people with schizophrenia or BD versus controls. However, most of the studies limited their outcomes to only weight loss and did not measure whether obesity surgery affected the status and treatment of psychiatric symptoms. Although few adverse events were reported among patients with BD, data from two studies demonstrated no significant deterioration of psychiatric symptoms post-surgery in people with schizophrenia.

Conclusions:

Growing evidence suggests that bariatric surgery may improve short-term weight status among people with BD. However, given the paucity of studies for schizophrenia, and the lack of information on medium-to long-term results, future large-scale high quality studies are required.

Key words: surgery for obesity; bariatric surgery; severe mental illness; psychosis; schizophrenia; bipolar disorder; antipsychotics.

INTRODUCTION

Schizophrenia or bipolar disorder (BD) are severe psychiatric disorders affecting about 1-2% of the worldwide population [1–3]. These severe mental illnesses are characterized by progressive and chronic deterioration of a wide variety of cognitive, psychosocial and physical functioning, which are associated with poorer outcomes. In particular, people with psychotic or bipolar disorder are at a 2-3 increased risk of developing metabolic disorders including obesity, diabetes, and hyperlipidaemia which accounts for the largest portion of the 10-20 years reduction in life expectancy [4,5]. The heightened cardiometabolic risk in this population is due to a combination of genetic factors, oxidative stress, socio-economic deprivation, lifestyle choices, eating disorders and metabolic effects of many psychotropic medications [4,5]. Whilst lifestyle interventions can improve cardio-metabolic outcomes to some degree, reducing weight on average by 3 kg in participating individuals [6], consistent long term data are lacking [7]. Pharmacological interventions such as metformin, also only appear to provide small to moderate improvements in metabolic outcomes in the short term [8].

In the general population, there is evidence that surgery for obesity is the most effective treatment for both weight loss and improving obesity-related physical comorbidities in severely obese individuals [9]. Recent literature has demonstrated that mental health conditions are very common among bariatric surgery patients—in particular, depression and binge eating disorder [10–15]. For example, in a recent sample of 393 obese patients, lifetime affective disorders, through structured clinical interview, were the most frequent diagnosis (total 64.9%; bipolar disorders 35.6% and depressive disorders 29.3%) [16]. In addition, a

study and literature review proposed a prevalence of BD in patients seeking bariatric surgery ranged from 0.4 to 1.7 for current BD and up to 3.5% for lifetime BD [11] [17].

However, little is known about the use and outcomes of bariatric surgery for patients with schizophrenia or BD. Indeed, much in line with other physical health care interventions, it appears that this patient population is not routinely offered surgical treatment.

This may in part be due to concerns about ability to adhere to the lifestyle changes required and whether that might impact effectiveness and safety, but there is little evidence to corroborate such assumptions. In addition, the risk of malabsorption of pharmacological treatment after surgery is an important limit and very few studies focused on psychotropic drugs monitoring after surgery [18]. In this paper, we conducted a systematic review to summarize the available knowledge on bariatric surgery in people with schizophrenia or BD, including information on the outcomes and safety of these procedures. Finally, we provide recommendations for future research.

METHODS

The current brief report systematic review did not follow specific criteria (e.g. PRISMA guidelines). To identify studies eligible for this work, we conducted a systematic literature search using the main scientific databases Embase, Medline and Psycinfo from inception until October 2016. Search terms included the following keywords grouped in various combinations: « (bariatric surgery or Roux-en-Y gastric bypass or sleeve gastrectomy or laparoscopic adjustable gastric band), and (schizophrenia or bipolar disorder) ». We also examined the reference sections from the selected papers to identify any additional relevant studies. Inclusion criteria were (a) studies published in an English-language peer-reviewed journal; (b) the study enrolled patients with schizophrenia or BD (defined according to

recognised criteria, e.g. DSM or ICD, medical diagnoses or validated questionnaire) and (c) considered bariatric surgery interventions.

Two authors conducted independently the searches, selected the included articles and then critically reviewed the included studies (YK and AA). Studies were synthesised with a narrative summary. We performed methodological quality assessment of included articles using the Newcastle Ottawa Scale (NOS). The NOS provides an assessment of the methodological quality of non-randomised trials and its content validity and reliability have been established [19]. Included studies are judged on 9 items across three key areas: selection of the participants, comparability of the participants and outcomes. Each study receives an overall score for methodological quality of up to 9 points (one for each item) and scores of 5 and above are considered to reflect satisfactory study quality. Full descriptive details of the included studies are reported in **Supplementary Figure 1**.

RESULTS

The electronic database searches identified 44 records from which 8 met our criteria. These eight studies addressed bariatric surgery outcomes among 279 people (mean age 44 years) with a psychiatric diagnosis of schizophrenia (n=14) or BD (n=265). The mean NOS score across the studies was 5.8 (range 5–6). Details of patient characteristics, surgical procedures, and timing of assessment are presented in **Table 1**. Of the 8 studies, 2 were prospective cohort studies and 6 involved a group control of patients without psychiatric diagnosis. The mean length of follow up was 15.7 months (range 12 to 24). Three studies reported information on patients with BD [20–22]; 1 reporting on schizophrenia patients [23]; and 4 studies reporting on both [24–27].

1) Weight and metabolic outcomes

Weight outcomes were reported in 7 studies (n= 135). In most studies, weight loss was reported as total weight loss (TWL) or as percent excess weight loss (% EWL), which are common metrics for reporting weight loss after bariatric surgery. All of these 7 studies found that patients diagnosed with schizophrenia or BD had achieved weight loss outcomes after bariatric surgery [20,22–27]. In the six comparative studies, weight loss was comparable among people with BD and schizophrenia (n= 117) and controls (n= 857) [20,22–24,26,27]. Taken together BD and schizophrenia patients had an average percent EWL ranged from -31% to -70% and was comparable to the general bariatric surgery population.

Regarding specifically schizophrenia patients, Hamoui et al. (n= 5) found no significant differences between schizophrenia patients and controls at 6 months, EWL was 39.5% (range 29.4%- 62.9%) in patients versus 46.9% (range 30.0%-95.5%) in controls [23]. Fuchs et al. found that the 4 schizophrenia patients had a 35.7% EWL and was comparable to patients without any psychiatric comorbidity at 1 year (p = 0.76) [26]. Finally, using 50% EWL as the standard for bariatric surgery success, all the 3 patients met this criterion in the non-controlled study of Shelby et al [25].

Regarding specifically BD patients, results of six studies (n=121) showed a significant mean EWL from baseline to 24 months, ranged from -31% to -70% [20,22,24–27].

One study examined weight change occurring greater than 24 months after surgery, and found no differences in weight between patients with BD and matched control patients who attended medical follow-up care at 24 months or longer (average of 52 months) after surgery [22]. Moreover, in a 12 months longitudinal study including BD (n=9) and

schizophrenia (n=4), psychiatric comorbidities did not affect EWL at any point of follow-up when adjusting for age, sex, race, gender, and type of operation [26].

Only three studies reported the prevalence of obesity-associated comorbidities including type 2 diabetes, cardiovascular disease, hypertension, and dyslipidaemia, among the patients but only at baseline [20,21,23]. However, none of the studies described the cardiometabolic outcomes after bariatric surgery.

2) Psychiatric outcomes

Only 3 studies described the psychiatric outcomes of patients who underwent bariatric surgery (n= 167) [21,23,25]. Reports of post-surgery psychiatric status have indicated no significant deterioration of psychiatric symptoms in 2 of 3 studies, in the year after surgery.

Very few patients with schizophrenia have been included in controlled or observational studies to date. In the study of Hamoui et al., no patient required psychiatric hospitalization following surgery and all continued to live at home with regular psychiatric follow-up [23]. In the non-controlled study of Shelby et al., the 3 schizophrenia patients experienced exacerbation of psychiatric problems such as agitation, paranoia, auditory hallucinations, and also medication changes. One required inpatient psychiatric hospitalization [25].

Obesity surgery studies in patients with serious mental illness mainly focused on BD. In a large study of 144 BD, patients who underwent bariatric surgery were compared with 1440 matched unexposed controls who were followed for a mean 2 years. The surgical intervention was not associated with significant differences in the risk of psychiatric hospitalization or change in rate of outpatient visits for psychiatric services [21]. In the non-controlled study of Shelby et al., among 7 BD patients with known postsurgery psychiatric

status (n=7/15), 6 patients suffered from symptom relapse and needed medication changes. Only one patient's decompensation was directly linked to malabsorption in the medical record. Six patients required inpatient psychiatric hospitalization [25].

3) Adherence and potential adverse events

One study reported physical adverse events in 2 patients among 5, each developed mild anaemia and mild hypocalcaemia), with a similar rate among controls [23]. In the study of Shelby, one patient's decompensation was directly linked to malabsorption in the medical record [25]. In another study of patients with a BD who had surgery, hospital re-admissions linked to bariatric surgery occurred in only 2 patients within 30 days of surgery (5.7%), both for nausea/vomiting and dehydration [22].

Concerning adherence, one study found no significant difference in the patients' adherence to the follow-up visits between patients with schizophrenia and BD and the controls [26]. In the study of Friedman et al, patients with BD attended follow-up care (medical and behavioral) at similar frequency as those without psychiatric disorder during the first year post-surgery, but were less likely to attend medical follow-up appointments 2 or more years post-surgery [22]. Finally, very low rates of loss to follow-up were reported among patients with BD and were not significantly different from the control group [21].

DISCUSSION

The preliminary results of the present review indicate that people with BD or schizophrenia can achieve successful short-term weight loss after bariatric surgery. Indeed, the excess weight loss was significant in either schizophrenia or BD patients and was comparable to weight loss for the general bariatric surgery population (6 studies). However, while there is a reasonable amount of data that support these findings for BD patients (n=265), current literature data is still lacking for schizophrenia patients (n=14). In addition, due to the limited follow-up of the included studies, we are unable to comment on the long-term outcomes.

Regarding psychiatric outcomes following surgery, one study (n=18) reported that 10 patients (BD, n=7, schizophrenia, n=3) suffered from some degree of exacerbation of their mental illness post-surgery, which is very high and of concern [25]. However, given the absence of a control group of non-surgical schizophrenia patients, these psychiatric courses and outcomes could not be compared in this study and we should be cautious in interpreting these findings. On the other hand, Ahmed et al. provided evidence that bariatric surgery does not adversely affect psychiatric course among stable patients with BD compared to controls. Interestingly, bariatric surgery has been associated with a significant decrease of the severity of depressive symptoms in one recent meta-analysis [15]. The potential favorable effect on the course and outcome of such psychiatric disorders after bariatric surgery remain to be studied. Indeed, in this context, bariatric procedures are generally provided to highly selected patients. Thus, due to this risk of selection bias, these findings should not be extrapolated to all schizophrenia or BD patients, particularly those who are highly incapacitated by their illness.

However, because individuals with schizophrenia or BD experience fluctuations of their symptoms throughout their lives, it should not be assumed, that exacerbations in psychiatric problems are negative outcomes due to the bariatric surgery itself. Indeed, the psychiatric functioning, severity of symptoms and stability seem of greater importance than attempting to differentiate the nuances of such complex diseases. According to an IFSO Consensus Statement, “surgery is a contraindication in cases of severe and untreated bipolar disorders, and in cases of unstable schizophrenia and psychosis” [9]. However, this should not be extrapolated to exclude patients with psychiatric disorders well stabilized and able to participate in treatment and long-term follow-up. Indeed, in the absence of a validated biomarker of psychiatric illness activity, symptomatic remission and functional restoration are the only available markers of wellness in psychiatry [28]. Interestingly, several standardized instruments have been developed to measure symptomatic [29] and functional remission [30,31] and can be used in routine clinical practice. Of importance, data from two studies showed that adherence was similar in people with psychosis versus controls and adverse events were few [26].

Some limitations need to be considered, including small sample size, particularly for schizophrenia patients for which data are nearly inexistent, and limited follow-up. Indeed, compared to patients with BD (n=265), the sample of schizophrenia patients was very low (n=14) and no strong conclusions can be drawn. Moreover, most of psychiatric diagnoses were based on clinical evaluations and only 3 studies used standardized assessment methods. Unfortunately, more specific details of the nature of the psychiatric diagnoses, the duration of disease and the drug management in these patients were missing. In addition, these studies limited their outcomes to only weight loss and did not measure whether obesity surgery affected the status and treatment of psychiatric conditions in these patients. Further studies addressing these specific psychopathological features are needed, including formal psychiatric

assessment, such as the PANSS (Positive and Negative Syndrome Scale). Finally, we did not assess the methodological quality of all studies in accordance with the PRISMA guidelines. Moreover, whilst we conducted a comprehensive search, it is possible that due to publication bias (in that studies with negative findings may be less likely to be published) could have influenced the available data. Clearly, future controlled and high quality studies are required before any firm conclusions can be made regarding the efficacy and safety of surgical interventions to manage obesity among people with BD or schizophrenia.

RECOMMENDATIONS FOR FUTURE RESEARCH

1) Psychological evaluation before bariatric surgery procedure

Little is established regarding psychiatric contraindications to bariatric surgery, and individual teams have their own psychiatric exclusion criteria [32]. Psychiatric disorders are often considered contraindications for bariatric surgery, especially psychosis, affective disorders, and personality disorders. Indeed, in a large survey, 31% of mental health professionals reported psychotic disorders as a specific psychiatric contraindication [33]. Moreover, one of the study included in our review, found that overall, patients diagnosed with BD have a relatively low rate for ultimately being approved for bariatric surgery (57%), and were less likely to be approved if they had a past psychiatric hospitalization [22].

Additionally, there are no uniform guidelines or protocols to guide the psychological assessment for bariatric surgery, clinical interviews forming the main psychological and psychiatric evaluation. Screening tools for cognitive function, mood disorders, eating disorders, as well as psychopathology tests, are not systematically used, but appear as very useful elements of the pre-surgical assessment. It must be remind that the functional impact of

psychiatric symptoms may vary considerably among individuals. Indeed, some people with psychosis disorders are able to function adequately in their daily lives, while others can be seriously impaired by their symptoms. The severity of psychiatric symptoms is more influential than the psychiatric diagnosis itself in determining surgery outcome [34]. Therefore, the relevant focus of the presurgical evaluation should be on the severity of psychiatric symptoms, the patient's functioning, the stability of the symptoms and the treatment in place. In this regard, other important outcomes that deserve further study in these patients are the influence of surgery and weight loss outcomes on the psychological health, quality of life, and comorbidities of these patients.

The physical health benefits may lead to consequent improvement in psychiatric symptoms. Longitudinal studies revealed significant and maintained improvements in psychopathology, quality of life, and self-esteem up to 4 years after obesity surgery [35,36]. Furthermore, recent data suggest that adherence to postoperative psychiatric follow-up is associated with greater postoperative weight loss in psychotic disorders [37].

Finally, patients with psychiatric disorders are at risk of the same medical complications of bariatric surgery as all other patients. Distress related to medical complications may however exacerbate psychiatric symptoms.

2) *Psychotropic medication management*

Literature regarding psychotropic pharmacokinetic changes in bariatric surgery patients is sparse [18]. Weight loss, nutritional status and short-term complications such as vomiting, diarrhoea and dehydration may induce changes in drug absorption, metabolism and response variability.

Growing data exists on the impact of obesity surgery on several drugs such as diabetic, hypertensive, and cardiac medications. A reduced drug absorption may occur post-bariatric surgery and this effect appears to be drug-specific [38]. However, little is known about the use of psychotropic medications after obesity surgery. Recent studies highlight the prevalence of antidepressant prescription use in patients before and after obesity surgery and support that patients are at risk for reduced drug bioavailability following surgery [39,40].

The studies to date do not provide sufficient knowledge on which to base recommendations for the management of psychotropic medications in bariatric surgery patients. For the malabsorptive procedures, most pharmacokinetic studies focused on Roux-en-Y gastric bypass (RYGB) with contradictory results. For the restrictive procedures, changes in drug absorption seem less likely to occur. However, some case reports have described severe lithium toxicity after RYGB and also after sleeve gastrectomy [41].

Thus, close psychiatric monitoring, individual dose-adjustment and therapeutic monitoring (blood level of drug) are highly recommended. Rigorously conducted controlled studies are needed to evaluate the effect of bariatric procedures on pharmacokinetic changes of psychotropic medication and other high-risk medications [18]. Finally, given the high risk of alcohol abuse/dependence and other addictive disorders following bariatric surgery, a referral to a specialist in addiction medicine should be also proposed [42,43].

CONCLUSION

People with schizophrenia or BD have extremely high levels of metabolic syndrome and obesity, which are leading contributors to the 15-year premature mortality gap. Obesity among patients with severe psychiatric illness predicts metabolic syndrome and cardiovascular risk, the most frequent cause of premature mortality in this patient subpopulation. Bariatric surgery may offer a promising option and may improve weight in

these patients with good adherence and few adverse events. However, the evidence base is in its infancy and no firm conclusions can be made regarding the efficacy and safety of bariatric surgery until high quality, controlled trials are conducted in people with schizophrenia and BD. Recommendations for implementation of future properly designed studies are summarized in the **table 2**.

Conflict of Interest Statement: The authors declare that there are no conflicts of interest in relation to the subject of this article.

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

Informed Consent: does not apply.

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Table 1: Selected studies measuring the metabolic and mental health conditions before and after bariatric surgery in people with schizophrenia or bipolar disorder

Study (Country)	NOS score	Psychiatric disorder and sample size	Diagnosis tool	Mean age, years	Group control if any	Surgical procedure (% or n)	Timing of assessment after surgery	Significant weight change	Psychological outcomes
Hamoui et al, 2004 (USA)	5	Schizophrenia (n= 5)	Clinical and psychological evaluation	40	165 consecutive morbidly obese patients without psychiatric diagnosis	DS: 3 SG: 1 BPD: 1	18 months	%EWL= 40*	No psychiatric hospitalization; patients continued psychiatric treatment
Steinmann et al, 2011. (USA)	6	Bipolar disorder (n=33)	Clinical and psychological evaluation	43	42 matched patients without psychiatric diagnosis	RYGB: 100%	1 year	%TWL = 31*	Concurrent psychiatric management during surgery
Ahmed et al, 2013. (USA)	6	Bipolar disorder (n=144)	Clinical and psychological evaluation	44	1,440 matched patients without psychiatric diagnosis	RYGB: 90% LAGB: 7% SG: 3%	1 year	NA	Bariatric surgery significantly improved psychiatric health in 1440 matched patients
Hayden et al, 2014 (Australia)	6	Bipolar disorder (n= 5) Schizophrenia (n= 1)	DSM-IV and SCID	45	93 patients without axis I psychiatric disorder	LAGB, 100%	2 years	%EWL= 40 to 57*	
Shelby et al, 2015 (USA)	5	Bipolar disorder (n=15) Schizophrenia (n= 3)	Clinical and psychological evaluation	43	No group control	RYGB: 66% LAGB: 17% SG: 17%	1 year	%EWL= 63	Postsurgery psychiatric hospitalization in 10 patients. Some exacerbation of psychiatric symptoms, yet weight loss
Fuchs et al, 2015 (USA)	6	Bipolar disorder (n=9) Schizophrenia (n= 4)	MADRS and CES-D	46	402 patients without any psychiatric history	LAGB: 77% SG: 23%	1 year	%EWL= 36*	No significant change in patients' adherence according to psychiatric treatment
Thomson et al, 2016 (Canada)	6	Bipolar disorder (n=17) Schizophrenia (n= 1)	MINI	44	126 patients without any psychiatric history	RYGB: 90% LAGB: 10%	1 year	%TWL = 36*	Mental illness and HRQOL burden
Friedman et al, 2016 (USA)	6	Bipolar disorder (n= 42)	Clinical and psychological evaluation	46	31 nonsurgical patients with bipolar disorder and 29 matched control surgical patients	RYGB: 90% LAGB: 10%	2 years	%EWL= 70*	

LAGB: laparoscopic adjustable gastric banding

SG: sleeve gastrectomy;

BPD: biliopancreatic diversion;

DS: duodenal switch operation

EWL: excess weight loss;

TWL: total weight loss;

* Comparable to the control group

NA: Not Applicable or Not provided

NOS score: the Newcastle Ottawa Scale, which provides an assessment of the methodological quality.

SCID: Structured Clinical Interview for Diagnostic

DSM-IV: Statistical Manual of Mental Disorders, 4th Edition

CES-D Center for Epidemiological Studies Depression

MADRS: Montgomery-Asberg Depression Rating Scale questionnaires

MINI: MINI International Neuropsychiatric Interview

Table 2: Recommendations for future studies

<ul style="list-style-type: none">• Multidisciplinary approach with access to liaison psychiatry/psychosomatic medicine and addiction medicine
<ul style="list-style-type: none">• Propose a screening use and psychiatric referral to characterize psychiatric diagnosis (ICD or DSM classification)
<ul style="list-style-type: none">• Use validated and easy reproducible scales to assess baseline mental health, such as the Positive and Negative Syndrome Scale (PANSS), the Beck Depression Inventory (BDI), the Three-Factor Eating Questionnaire (TFEQ), the Binge Eating Scale (BES) ...
<ul style="list-style-type: none">• Ensure studies with long-term follow-up (i.e. > 5 years)
<ul style="list-style-type: none">• Assess adherence to bariatric postoperative guidelines and engagement in the follow-up
<ul style="list-style-type: none">• Offer adherence intervention session
<ul style="list-style-type: none">• Attend closely to the management of psychotropic medications, altering dose if needed, monitoring of plasma concentration
<ul style="list-style-type: none">• Continue a close follow-up with a psychiatrist following surgery, with a particular assessment of substance use disorders
<ul style="list-style-type: none">• Continue postoperative dietary and psychological support
