

Association of Components of Metabolic Syndrome with Depression and Anxiety in Patients Undergoing Weight Reduction Surgery

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Abstract: *Background:* Obesity can be associated with psychiatric disorders such as depression. *Aim:* To determine the prevalence and association of psychiatric disorders in patients with excess body weight. *Methods:* Patients scheduled for weight reduction surgery were included. For each patient, pre-surgical clinical and psychiatric data were collected. Follow-up data were available 1-year after surgery. Patients with psychiatric disorders were compared to those without psychiatric disorders. Mann-Whitney non-parametric test was used for comparison of numerical parameters, while prevalence of certain clinical and demographic events were validated using chi-square homogeneity test. *Results:* 499 patients were included: age: 42.8 ± 11.0 years, 20% male, 76% Caucasians, BMI 46.8 ± 10.8 , ALT 32.5 ± 21.7 and AST 25.0 ± 14.3 . At baseline, a history of psychiatric disorder was documented in 214 (43%) patients (depression in 35% of patients, anxiety in 6% and other psychiatric diagnosis in 2.2%). Patients with a history of depression were older ($p=0.0021$), more likely to report a history of drinking alcohol either at baseline ($p=0.0434$) or 1-year after surgery ($p=0.0302$), and more likely to be female ($p=0.0079$) and Caucasian ($p=0.0096$) than patients without psychiatric history. The depression cohort of this study also had significantly higher triglyceride levels ($p=0.0492$) than any other psychiatric diagnosis cohort, and the highest rates of hyperlipidemia ($p=0.012$) and hypertension diagnoses ($p=0.0074$) out of all cohorts, including the cohort of subjects never diagnosed with a psychiatric disorder. *Conclusions:* Patients undergoing weight reduction surgery seem to have high prevalence of depression and anxiety. Patients previously diagnosed with depression also appear to have a significantly higher rate of hypertension and hyperlipidemia than patients who were never diagnosed with a psychiatric disorder.

Keywords: Depression, hypertension, hyperlipidemia, morbid obesity, weight reduction surgery.

INTRODUCTION

Obesity is becoming increasingly prevalent in the United States with over 30% of the population being considered obese, affecting over 93 million people [1-3]. Additionally, obesity enhances the negative impact of alcohol to the liver [4]. The prevalence of obesity-associated complications is expected to rise along with the weight reduction surgery procedures that have become an accepted treatment option for some patients. In expert hands, weight reduction surgery procedures are generally well tolerated and one of the fastest growing surgeries in the United States [5, 6]. In addition to weight loss, a decrease in risk factors associated with metabolic syndrome and its complications such as non-alcoholic fatty liver disease (NAFLD), sleep apnea, hypertension, diabetes mellitus, and hyperlipidemia with weight reduction surgery has led to an improvement in health status for many patients [6,7].

Although weight reduction surgery can be effective in most patients, factors such as binge eating, abnormal energy metabolism, and psychosocial functioning can negatively affect outcomes [8-14]. Furthermore, there is some early data suggesting that post weight reduction surgery, patients may consume excessive amounts of alcohol [15, 16].

Only limited research has addressed psychiatric issues in obese and morbidly obese patients. One study found that patients with lifelong depression and anxiety were significantly more likely to smoke, drink heavily, become physically inactive and obese [17]. Another study with overweight men suggested that there is an association between panic disorder and underlying heart disease or diabetes mellitus [18]. Levels of mortality for obesity-related conditions such as coronary heart disease have also been found to be higher in patients with either schizophrenia or depression [19]. All these studies suggest an association between psychiatric conditions and components of metabolic syndrome such as obesity, hyperlipidemia, hypertension and type II diabetes. The aim of our study was to assess a history of psychiatric diagnoses and determine its independent predictors in a cohort of patients undergoing weight reduction surgery.

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MATERIALS AND METHODOLOGY

Patients with an established diagnosis of morbid obesity who were eligible and scheduled for weight reduction surgery were identified from our database. Eligibility for weight reduction surgery required a physical and psychiatric evaluation pre-surgery. Patients must have been deemed as being in a stable state mentally and physically to be eligible for bariatric surgery. Any patient who was evaluated and deemed not eligible for surgery at the time is referred for additional management and was not eligible for this study. Active alcohol abuse (20 gm/day or greater) was also an exclusion criteria for surgery and for this study. For each patient extensive clinical (e.g. disease severity, body mass index), demographic (e.g. gender, age, ethnicity, medical history), pre-operative assessments (e.g. psychiatric and alcohol intake history) and laboratory data were available. A liver biopsy had been obtained during surgery and read by a single hepatopathologist in a standardized manner. Additionally, extensive data was available after weight reduction surgery (e.g. metabolic syndrome components, body mass index, alcohol intake, etc.).

Psychiatric disorders were classified into five groups:

- Depression (included depression of any type, bipolar disorder, and also post-partum and seasonal depressive disorders)
- Anxiety (any anxiety including panic disorder and PTSD)
- Alcohol abuse
- Eating disorder (including anorexia and bulimia)
- Schizophrenia

The study was approved by our institutional review board.

STATISTICAL ANALYSES

The prevalence of psychiatric diagnoses and alcohol consumption in the candidates for weight reduction surgery were determined. Independent predictors of excessive alcohol consumption after weight reduction surgery as well as those for psychiatric diagnoses were also assessed.

Wilcoxon and Kruskal-Wallis nonparametric tests were conducted for group comparisons. All tests were two-tailed, and p-values not exceeding 0.05 were considered significant.

Table 1. Comparison of Patients Undergoing Weight Reduction Surgery with any Psychiatric Diagnosis History to those without a Psychiatric Diagnoses

	Entire Cohort	Any Psychiatric Diagnosis History	No Psychiatric Diagnosis History	P-value*
N	498	214	284	
Prevalence	100%	42.97%	57.03%	
Age (Years)	42.8 ± 11.0	44.5 ± 11.2	41.5 ± 10.7	0.0028
Gender (%Male)	20.2%	14.62%	24.46%	0.0072
Caucasian	76.31%	81.31%	72.54%	0.0226
African American	15.46%	11.21%	18.66%	0.0229
Hispanic	2.61%	2.34%	2.82%	0.7392
Asian	0.4%	0%	0.7%	0.2202
Diabetes Mellitus	26.14%	30.48%	22.79%	0.057
Hyperlipidemia	44.19%	50.24%	39.47%	0.0193
Hypertension	53.38%	59.71%	48.51%	0.0154
BMI	46.8 ± 10.8	46.2 ± 11.9	47.2 ± 9.9	0.4002
Waist	133.3 ± 21.8	132.0 ± 22.1	134.3 ± 21.5	0.3895
ALT	32.5 ± 21.7	30.6 ± 17.0	34.0 ± 24.7	0.5469
AST	25.0 ± 14.3	24.4 ± 10.9	25.4 ± 16.4	0.3916
AST/ALT	0.9 ± 0.3	0.9 ± 0.3	0.8 ± 0.3	0.0918
Glucose	106.9 ± 39.0	105.7 ± 36.1	107.8 ± 41.1	0.3303
Cholesterol	194.3 ± 39.2	197.8 ± 41.8	191.6 ± 37.0	0.3019
Triglycerides	165.6 ± 114.1	178.5 ± 147.1	156.1 ± 80.8	0.1272
Alcohol Intake Before Weight Reduction Surgery	47.15%	51.71%	43.66%	0.0822
Alcohol Intake 1 Year Post Weight Reduction Surgery	6.14%	10%	3.62%	0.0499
Smoking	9.28%	9.39%	9.18%	0.9423
Liver biopsy showing fatty liver disease	93.57%	92.9%	94.04%	0.6602
Liver biopsy showing hepatic fibrosis	16.45%	15.09%	17.43%	0.5455
Liver biopsy showing steatohepatitis	21.66%	17.31%	24.77%	0.084

*P-value of the difference between 'Any Psychiatric Diagnosis History' and 'No Psychiatric Diagnosis History'.

Means and variances for patients from the five psychiatric groups were described, and all patients with any psychiatric history were merged into the cohort “Any psych” (presence of any psychiatric history) to compare with the “No Psych” (no presence of psychiatric history) group. Each psychiatric cohort was then compared separately (namely, “Depression”, “Anxiety”, “Alcohol abuse”, “Eating Disorder”, “Schizophrenia”) with the “None” cohort. A comparison of patients who reported drinking alcohol and patients without a history of significant alcohol consumption was also conducted.

Additional analyses were done to determine factors independently associated with the presence of a psychiatric diagnosis history (presence of any psychiatric history), and presence of recent alcohol use history parameters using multiple regression analysis with stepwise (bi-directional) selection of variables for both parameters were performed. In the model annotations, positive beta values represent direct proportionality, and negative beta values represent inverse proportionality.

RESULTS

Patient Population

Four hundred ninety-nine patients were included [age: 42.8 ± 11.0, 20% male, 76% Caucasians, BMI 46.8 ± 10.8, ALT 32.5 ± 21.7 and AST 25.0 ± 14.3] (Table 1). At baseline, a history of psychiatric disorder was documented in 214 (43%) patients (depression in 35% of patients, anxiety in 6% and other psychiatric diagnosis in 2%) (Table 2).

The sub-cohort of patients with a history of psychiatric disorder were older (p= 0.0028), more likely to be female (p=0.0072), had a higher prevalence of both hyperlipidemia (p= 0.0193) and hypertension (p= 0.0154) than patients without a history of psychiatric disorder. Those with history of psychiatric diagnosis were also more likely to report alcohol use on follow-up post weight reduction surgery (p= 0.0499) (Table 1).

Compared to those who reported no history of psychiatric diagnosis, morbidly obese patients who reported a history of

Table 2. Means and Variances for Patients with a History of Five Psychiatric Diagnoses

Psychiatric Diagnosis Subtypes	Depression	Anxiety	Alcohol Abuse	Eating Disorder	Schizophrenia	Any Psychiatric Diagnosis History
N	172	31	5	5	1	214
Prevalence	34.54%	6.22%	1%	1%	0.2%	42.97%
Age	44.8 ± 11.2	43.0 ± 10.7	44.5 ± 13.8	42.2 ± 13.6	55.0 ± 0.0	44.5 ± 11.2
Gender (% Male)	14.04%	16.13%	25%	20%	0%	14.62%
White Caucasian	83.14%	80.65%	60%	60%	0%	81.31%
Black African American	11.05%	9.68%	20%	20%	0%	11.21%
Hispanic	2.91%	0%	0%	0%	0%	2.34%
Asian	0%	0%	0%	0%	0%	0%
Diabetes Mellitus	27.81%	48.39%	0%	40%	0%	30.48%
Hyperlipidemia	51.81%	45.16%	25%	40%	100%	50.24%
Hypertension	61.68%	55.17%	50%	20%	100%	59.71%
BMI	45.8 ± 11.8	47.6 ± 13.0	51.4 ± 11.8	46.4 ± 12.9	35.1	46.2 ± 11.9
Waist	131.8 ± 21.5	130.0 ± 25.3	138.9 ± 26.8	144.1 ± 24.6	123	132.0 ± 22.1
ALT	30.4 ± 17.5	30.6 ± 13.7	28.0 ± 1.4	41.0 ± 19.4	18	30.6 ± 17.0
AST	23.9 ± 10.3	23.1 ± 7.7	55.0 ± 36.8	37.2 ± 14.5	16	24.4 ± 10.9
AST/ALT	0.9 ± 0.3	0.8 ± 0.3	2.0 ± 1.4	0.9 ± 0.2	0.9	0.9 ± 0.3
Glucose	106.2 ± 37.9	105.9 ± 27.8	89.7 ± 6.7	95.3 ± 19.0	NA	105.7 ± 36.1
Cholesterol	198.8 ± 42.4	201.0 ± 34.8	159.3 ± 5.1	187.3 ± 59.6	134.0 ± 0.0	197.8 ± 41.8
Triglycerides	185.6 ± 158.2	158.9 ± 74.8	114.0 ± 49.4	110.0 ± 23.9	83.0 ± 0.0	178.5 ± 147.1
Alcohol Intake Before Weight Reduction Surgery	53.66%	41.94%	50%	40%	100%	51.71%
Alcohol Intake 1 Year Post Weight Reduction Surgery	11.27%	6.67%	0%	0%	0%	10%
Smoking	7.53%	20%	25%	0%	0%	9.39%
Liver biopsy showing fatty liver disease	92.97%	100%	75%	66.67%	100%	92.9%
Liver biopsy showing hepatic fibrosis	13.74%	21.05%	50%	0%	0%	15.09%
Liver biopsy showing steatohepatitis	16.28%	26.32%	25%	0%	0%	17.31%

depression were significantly older ($p=0.0021$), more likely to be female ($p=0.0079$), Caucasian or African American ($p=0.0096$, $p=0.0307$, respectively), had higher incidence of hyperlipidemia ($p=0.012$), hypertension ($p=0.0074$), and high triglycerides ($p=0.0492$). Patients reporting a history of depression were also significantly more likely to report excessive alcohol consumption in the past ($p=0.0434$) and upon follow-up post weight reduction surgery ($p=0.0302$) (Table 2, 3). There was no significant difference found in BMI between subjects with a history of any psychiatric disorder and subjects without a psychiatric diagnosis (Tables 1-2).

Patients with a reported history of anxiety, when compared to patients without any psychiatric diagnosis, were significantly more likely to have diabetes ($p=0.0019$). A correlation was also seen between history of Eating Disorder and AST ($p=0.0254$) (Table 3). No significant differences were seen between patients without a psychiatric history, and patients with history of schizophrenia and alcohol abuse (Tables 2, 3).

Association of Psychiatric Disorders and Alcohol Consumption with Clinico-demographic Variables

Although a number of clinical and demographic variables were found to correlate significantly for the overall cohort with psychiatric diagnoses, there was no overlap in significant variables between these groups. Age ($p=0.0028$), gender ($p=0.0072$), Caucasians ($p=0.0226$), African Americans ($p=0.0229$), hyperlipidemia ($p=0.0193$), and hypertension ($p=0.0154$) correlated significantly with any history of psychiatric diagnosis (Table 1). In analysis of dichotomous variables (recent alcohol use history, gender, diabetes mellitus, hyperlipidemia and elevated AST/ALT), only elevated AST/ALT was found to be significantly associated in the prediction model with the presence of psychiatric diagnosis history ($p=0.0198$). ALT ($p=0.0264$) and alcohol intake at follow-up post weight reduction surgery ($p=0.0126$) were significantly correlated with recent alcohol use history prior to weight reduction surgery. Neither ALT nor alcohol intake pre weight reduction surgery were significant for the overall psychiatric diagnosis cohort (Table 1).

Table 3. Comparison of each Psychiatric Diagnosis Cohort to Patients with No Psychiatric Diagnosis
P-values (Compared to No Psychiatric Diagnosis Cohort)

	Depression	Anxiety	Alcohol Abuse	Eating Disorder	Schizophrenia
Age	0.0021	0.4737	0.6159	0.9817	0.1915
Gender	0.0079	0.3003	0.9801	0.8179	0.5759
White Caucasian	0.0096	0.3323	0.5346	0.5346	0.1081
Black African American	0.0307	0.2141	0.9393	0.9393	0.6391
Hispanic	0.9553	0.3466	0.7111	0.7111	0.8818
Asian	0.2719	0.6452	0.8657	0.8657	0.9665
Diabetes Mellitus	0.2351	0.0019	0.281	0.3657	0.5938
Hyperlipidemia	0.012	0.5408	0.5563	0.981	0.2207
Hypertension	0.0074	0.4952	0.9527	0.2062	0.3082
BMI	0.2142	0.5387	0.5915	0.5661	0.1119
Waist	0.2816	0.9145	0.7525	0.4462	0.5416
ALT	0.4116	0.9973	0.974	0.1942	0.3361
AST	0.6462	0.7259	0.0664	0.0254	0.3443
AST/ALT	0.1218	0.9563	0.0561	0.1923	0.5272
Glucose	0.3063	0.7459	0.2717	0.5887	NA
Cholesterol	0.1989	0.3378	0.0706	0.4271	0.1275
Triglycerides	0.0492	0.6646	0.3633	0.2087	0.2112
Alcohol Intake Before Weight Reduction Surgery	0.0434	0.8548	0.7996	0.8702	0.2611
Alcohol Intake 1 Year Post Weight Reduction Surgery	0.0302	0.5641	0.8772	0.8058	0.8772
Smoking	0.5853	0.0933	0.2846	0.4834	0.7639
Liver biopsy showing fatty liver disease	0.6943	0.2765	0.1206	0.0532	0.8166
Liver biopsy showing hepatic fibrosis	0.363	0.6918	0.0931	0.3633	0.6555
Liver biopsy showing steatohepatitis	0.0633	0.8812	0.9916	0.3255	0.5745

Table 4. Comparison of Patients with and without Alcohol Intake before Weight Reduction Surgery

	Alcohol Intake Before Weight Reduction Surgery		P-value
	Yes*	No	
N	223	250	
Prevalence	44.78%	50.2%	
Age	42.6 ± 10.7	42.9 ± 11.3	0.7818
Gender (Male)	19.28%	20.88%	0.6649
White Caucasian	79.82%	74.4%	0.1623
Black African American	13%	18%	0.1355
Hispanic	2.69%	2.4%	0.841
Others	0.45%	0.4%	0.9354
Diabetes Mellitus	26.13%	25.4%	0.858
Hyperlipidemia	44.75%	42.39%	0.6091
Hypertension	50.46%	55.1%	0.3177
BMI	45.7 ± 10.7	47.7 ± 10.9	0.0248
Waist	131.3 ± 21.7	135.4 ± 21.9	0.3636
ALT	34.7 ± 26.6	30.1 ± 16.1	0.2629
AST	25.3 ± 16.1	24.4 ± 12.3	0.8285
AST/ALT ratio	0.8 ± 0.3	0.9 ± 0.3	0.1095
Glucose	105.1 ± 33.9	107.6 ± 42.0	0.4461
Cholesterol	193.0 ± 38.7	195.8 ± 39.4	0.5631
Triglycerides	154.3 ± 84.7	173.0 ± 132.3	0.1034
Psychiatric Diagnosis	48.53%	39.6%	0.0093
Alcohol Intake 1 Year Post Weight Reduction Surgery	10.81%	2.74%	0.0128
Smoking	10.86%	6.29%	0.1236
Liver biopsy showing fatty liver disease	95.27%	91.75%	0.1935
Liver biopsy showing hepatic fibrosis	18%	15.87%	0.5937
Liver biopsy showing steatohepatitis	18.24%	24.15%	0.1827

* Some alcohol intake reported; less than 2 drinks (20 gm/day) per eligibility criteria for surgery.

Additionally, alcohol consumption history was also studied. Of the morbidly obese patients who participated in this study, 45% (N=223) reported history of alcohol consumption (Table 4). The majority of these patients (98.7%) reported 0-2 drinks of alcohol per day, and only 3 patients reported >2 drinks per day. Morbidly obese patients who reported a history of alcohol consumption were more likely to also report a history of psychiatric disorders (48.5% vs. 39.6%, $p=0.0093$). Of the entire cohort of morbidly obese patients 46.6% reported some alcohol consumption at the time of their evaluation for weight reduction surgery. Of this cohort only 10.81% reported alcohol consumption post surgery. On the other hand, 52.8% of the entire cohort did not report any alcohol consumption. After surgery 2.74% of this group reported some alcohol intake on the 1-year follow-up (Table 4). Furthermore, those who reported a history of alcohol consumption at baseline were more likely to drink 1-year after weight reduction surgery (10.81% vs. 2.74%, $p=0.0128$) (Table 4). In multivariate analysis, predictors of alcohol consumption were a history of psychiatric disorders, younger age and lower AST/ALT ratio (model p -

value=0.02039). The only variable in the predictive modeling that was significant for presence of recent alcohol use was also AST/ALT ratio ($p=0.0282$).

DISCUSSION

Associations of age, gender, ethnicity, and alcohol use with depression are known in the obesity literature [17-22] as well as in wider research on depression. Our data is consistent with this previously reported data [21]. In general, the high rate of depression in our patient population scheduled for weight reduction surgery was not surprising given previous research in this area. A study which looked specifically at depression and anxiety found that patients with lifelong depression were significantly more likely to smoke, binge drink, drink heavily, be physically inactive, and be obese than those without this diagnosis [17]. This same study noted a form of dose-response curve between these above-mentioned conditions with both severity of

depression and history of depression (never depressed, previously depressed, and currently depressed) [17].

In this study, the majority of patients with a history of psychiatric disorder carried the diagnosis of depression (Table 2). All patients who reported a history of depression in this study met all the criteria to proceed with weight reduction surgery. Since patients with severe depression are not candidates for weight reduction surgery, our patients were either only mildly depressed or not depressed at the time of surgery. Assessing our patients with history of psychiatric conditions (such as a history of depression) provided some interesting clinical associations (Tables 2 and 3).

Our data also indicated that our patients with a history of depression, had significantly higher triglyceride levels ($p=0.0492$), diagnosis rates for hyperlipidemia ($p=0.012$) and hypertension ($p=0.0074$). These factors are components of metabolic syndrome. On the other hand, patients with a history of depression did not have the highest BMI or the greatest waist circumference (Table 3). A meeting summary for the National Institute of Mental Health (NIMH) concluded that levels of mortality for obesity-related conditions such as coronary heart disease are higher in patients with either schizophrenia or depression [19]. This is consistent with our findings since our patients scheduled for weight reduction surgery has significantly higher levels of hypertension and hyperlipidemia, both risk factors for coronary heart disease.

Diagnosis of anxiety disorder was the second most common psychiatric disorder in our study and has previously been associated with obesity as well. As mentioned above, a study which looked specifically at depression and anxiety found that patients with lifelong anxiety were significantly more likely to smoke, drink, and become physically inactive and obese [17]. Our study suggests a significant correlation between anxiety in morbidly obese patients and type 2 diabetes. The significant correlation between diabetes mellitus and diagnosed anxiety does have some corroborating support. One study has suggested that in overweight men, those diagnosed with panic disorder should be screened for diabetes mellitus and underlying heart disease [28].

Another interesting finding of our study was that patients who reported alcohol use before weight reduction surgery had a significantly lower BMI than patients without alcohol use at baseline (Table 4). Although a number of studies have been conducted to address questions regarding changes in alcohol consumption before and after weight reduction surgery, baseline weight of patients who reported some consumption of alcohol before weight reduction surgery to patients who did not consume alcohol prior to surgery is not described [23-28]. Further research is needed in this area to determine the reasons for this association. In our study, those who consumed alcohol prior to weight reduction surgery were also the most likely to drink alcohol after weight reduction surgery. This finding is consistent with previous findings [15]. Additionally, although not significantly different, those who consumed alcohol prior to weight reduction surgery were more likely to have elevated ALT (Table 3). This finding may suggest the damaging impact of alcohol in this group.

A correlation was also found between the group diagnosed with an eating disorder and AST. In the literature, certain eating disorders can cause transaminitis, including anorexia, bulimia and eating disorder not otherwise specified [29-31]. However, a large study of patients with eating disorders determined that hepatic dysfunction was not common among eating disorders and liver damage could often be attributed to low weight [32]. Conversely, with our high BMI weight reduction surgery candidates, excess weight and undiagnosed non-alcoholic fatty liver disease or non-alcoholic steatohepatitis which are the hepatic manifestations of metabolic syndrome, may be responsible for the elevation of AST in this population.

One limitation for our study was that our study population did not have a follow up liver biopsy as well as extensive post operative psychiatric assessment. Nevertheless, the large cohort of patients included and in-depth clinical, psychiatric and laboratory data provide strength to this study.

CONCLUSIONS

In summary, our study suggests a possible link between a history of depression and or anxiety in patients undergoing weight reduction surgery with components of metabolic syndrome. Patients undergoing weight reduction surgery seem to have high prevalence of depression and anxiety. Patients previously diagnosed with depression also appear to have a significantly higher rate of hypertension and hyperlipidemia than patients who were never diagnosed with a psychiatric disorder. Nevertheless, future research, both to confirm these findings and provide possible mechanisms for these relationships will be important.

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