Leorides Severo Duarte Guerra

**Perfil psicopatológico de pacientes com obesidade candidatos
à cirurgia bariátrica: análise de classes latentes e fatores
associados**

Tese apresentada à Faculdade de Medicina da
Universidade de São Paulo para obtenção de
título de Doutor em Ciências

Programa de Psiquiatria

Orientador: Prof. Dr. Wang Yuan Pang

(Versão corrigida. Resolução CoPGr 6018/11, de 1 de novembro de 2011. A versão original está
disponível na Biblioteca da FMUSP)

**São Paulo
2019**

Dados Internacionais de Catalogação na Publicação (CIP)

Preparada pela Biblioteca da
Faculdade de Medicina da Universidade de São Paulo

©reprodução autorizada pelo autor

Guerra, Leorides Severo Duarte
Perfil psicopatológico de pacientes com obesidade
candidatos à cirurgia bariátrica : análise de
classes latentes e fatores associados / Leorides
Severo Duarte Guerra. -- São Paulo, 2019.
Tese(doutorado)--Faculdade de Medicina da
Universidade de São Paulo.
Programa de Psiquiatria.
Orientador: Wang Yuan Pang.

Descritores: 1.Obesidade 2.Cirurgia bariátrica
3.Transtornos mentais 4.Psicopatologia 5.Análise de
classe latente 6.Comorbidade

USP/FM/DBD-009/19

Responsável: Erinalva da Conceição Batista, CRB-8 6755

*Aos meus filhos Priscila e
Gustavo Duarte Guerra*

AGRADECIMENTOS

Meus agradecimentos a todos que acreditaram e participaram dessa pesquisa. Cada um em etapas e de formas diferentes. Minha resiliência e persistência, ressaltada por todos, não teriam êxito sem o estímulo e apoio que recebi ao longo do percurso acadêmico. Assim, meu muito obrigada:

Ao Prof. Dr. Wang Yuan Pang, meu dedicado orientador, hoje, especial amigo. Obrigada pelo carinho, paciência, pelo estímulo constante e por acreditar que seria possível!

Ao Prof. Dr. Francisco Lotufo Neto, pelo estímulo constante e apoio.

Ao Prof. Dr. Marco Aurélio Santo, pela cordialidade em abrir as portas do Centro de cirurgia bariátrica e confiança em meu trabalho.

À Nestor J. Guerra, pelo companheirismo e suporte familiar.

Ao Dr. Bruno M. Coêlho, querido colega que ganhei nesta jornada, pelo seu apoio.

À Regina Maria R. Morin, pelo apoio constante e especial amizade.

À Celina Sobreira, Luciléia Gonçalves, Patrícia Silva, Paula Medeiros e Cecília Belfant (in memorian), agradeço a todas pela dedicação e pelo profissionalismo na coleta dos dados.

À Aline Damasceno, pela paciência e habilidade no ensino da estatística.

À Elisa Fukushima e Isabel Ataíde, secretárias da pós-graduação, pela presteza e pelo profissionalismo.

Aos professores Renério Fráguas Jr., Alexandre A. Loch e Beatriz H. Carvalho Tess, pelos apontamentos na qualificação.

Minha reverência a todos os participantes dessa amostra que, gentilmente, superaram suas dificuldades e atenderam ao meu convite. Dificuldades que, muitas vezes, me causaram comoção diante de tanta disponibilidade de participação. Os resultados desta pesquisa mostraram que muitos comportamentos estigmatizados do paciente com obesidade, são sintomas de graves transtornos psiquiátricos, que merecem especial atenção. Desta forma, espero ter contribuído para melhor compreensão desta complexa e incapacitante doença, e que novos tratamentos possam trazer melhor qualidade de vida a todos com obesidade. Desta forma, a todos vocês, meu muitíssimo obrigada.

Esta pesquisa contou com o apoio da **Fundação de Amparo à Pesquisa do Estado de São Paulo – FAPESP**.

Auxílio pesquisa Processo 2012/17435-7.

Bolsa de Mestrado Processo 2012/17498-9.

E apoio da **Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES)** – Código de Financiamento 001.

“Nenhuma experiência é, em si, a causa do nosso sucesso ou fracasso. Nós não sofremos do choque de nossas experiências, o chamado trauma, mas o transformamos em algo que atende aos nossos propósitos. Não somos determinados por nossas experiência, mas o sentido que damos a elas é autodeterminante.”

Alfred Adler

NORMALIZAÇÃO ADOTADA

Esta tese está de acordo com as seguintes normas, em vigor no momento desta publicação: Referências: adaptado de *International Committee of Medical Journals Editors* (Vancouver).

Universidade de São Paulo. Faculdade de Medicina. Serviço de Biblioteca e Documentação. Guia de apresentação de dissertações, teses e monografias. Elaborado por Anneliese Carneiro da Cunha, Maria Julia de A.L. Freddi, Maria F. Crestana, Marinalva de Souza Aragão, Suely Campos Cardoso, Valéria Vilhena. 2ª Ed. São Paulo: Serviços de Biblioteca e Documentação; 2005.

Abreviaturas dos títulos dos periódicos de acordo com *List of Journals Indexed in Index Medicus*.

A ortografia da Língua Portuguesa adotada está conforme o Acordo Ortográfico da Língua Portuguesa, assinado em Lisboa, em 16 de dezembro de 1990, por Portugal, Brasil, Angola, São Tomé e Príncipe, Cabo Verde, Guiné-Bissau, Moçambique e, posteriormente, por Timor Leste. Decreto Legislativo Brasileiro nº 54, aprovado em 18 de abril de 1995 e em vigor desde 1º de janeiro de 2009.

SUMÁRIO

Lista de abreviaturas

Resumo

Abstract

1.	INTRODUÇÃO.....	01
2.	REVISÃO DA LITERATURA.....	05
2.1.	Obesidade	06
2.2.	Doenças neuropsiquiátricas e obesidade.....	08
2.3.	Curso e comorbidade dos transtornos psiquiátricos.....	10
2.4.	Subgrupos de apresentação psicopatológica em obesidade.....	12
2.5.	Hipóteses	14
2.6.	Objetivos.....	15
3.	MÉTODO E CASUÍSTICA.....	16
3.1.	Tipo de estudo.....	17
3.2.	Estudo base “Frequência de transtornos mentais em pacientes obesos candidatos a cirurgia bariátrica por meio de entrevista estruturada para transtornos do DSM-IV (SCID-I/P)”	17
3.2.1	Sujeitos da amostra	18
3.2.2.	Instrumentos de avaliação	19
3.2.3.	Procedimentos	20
3.2.3.1	Recrutamento	20
3.2.3.2	Entrevistadores	21
3.2.3.3	Participantes	21
3.2.3.4	Aplicações	21
3.3	Análise estatística.....	22
3.4.	Aspectos Éticos.....	25
4.	RESULTADOS	27
4.1.	Artigo I - <i>Morbidity persistence and comorbidity of mood, anxiety, and eating disorders among preoperative bariatric patients</i>	28
4.1.1	Discussão artigo I.....	35
4.2	Artigo II - <i>Gender-related patterns of psychiatric disorder clustering among surgery candidates: A latent class analysis</i>	38
4.2.2	Discussão artigo II.....	46
5.	DISCUSSÃO	49
6.	CONCLUSÃO.....	55
7.	ANEXOS.....	58
	A - Aprovação pelo Comitê de Ética.....	59
	B - Anuência Interdepartamental.....	60
	C - Termos de consentimento livre informado.....	61
	D - Questionário Clínico.....	65
	E - <i>Structured Clinical Interview for DSM-IV Axis I Diagnosis-SCID</i>	66
8.	REFERÊNCIAS BIBLIOGRÁFICAS.....	67
9.	APÊNDICE: Produção Científica.....	77

LISTA DE ABREVIATURAS – SIGLAS - SÍMBOLOS

ABNT	Associação Brasileira de Normas Técnicas
SCID	<i>Structured Clinical Interview for DSM-IV Axis I Diagnosis</i>
CAPPesq	Comissão de ética para avaliação de projeto de pesquisa
DSM	Manual de Diagnóstico e Estatística de Transtornos Mentais
HC-FMUSP	Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo
OMS	Organização Mundial de Saúde
NESARC	<i>National Epidemiological Study of Alcohol and Related Conditions</i>
IMC	Índice de Massa Corporal
IPq-HC	Instituto de Psiquiatria do Hospital das Clínicas
FMUSP	Faculdade de Medicina da Universidade de São Paulo
RP	Razão de prevalência
1M/LT	Transtornos atuais/Transtornos ao longo da vida
Vol.	Volume
p.	Página
ACL	Análise de classe latente
Nov.	Novembro
Ex.	Exemplo
Fig.	Figura
EUA	Estados Unidos da América
LABS	<i>Longitudinal assessment of bariatric surgery</i>
Cols.	Colaboradores
DNT	Doenças não Transmissíveis
FAPESP	Fundação de amparo à pesquisa do estado de São Paulo
IC	Intervalo de Confiança
N	Número da Amostra
SPSS	<i>Statistical Package for the Social Sciences</i>
Stata	<i>Software for statistics and data science</i>
TCA	Transtornos de compulsão alimentar
TA	Transtornos alimentares

GAF	<i>Global Assessment of Functioning</i>
TB	Transtorno Bipolar
TBSOE	Transtorno Bipolar sem Origem Específica
www	Rede Mundial de Computadores (do Inglês, <i>World Wide Web</i>)
kg/m²	Quilograma por metro quadrado
%	Porcentagem
≥	Sinal de igual/maior
<	Sinal de menor
AIC	<i>Akaike information criterion</i>
BIC	<i>Bayesiano information criterion</i>
aBIC	<i>Bayesiano information criterion ajustado</i>
VLMR	<i>Vuong-Lo-Mendell-Rubin</i>
LMR	<i>Lo-Mendell-Rubin</i>
TRV	Teste de razão de verossimilhança
<i>P</i>	Coefficiente de correlação de Pearson

RESUMO

Guerra LSD. *Perfil psicopatológico de pacientes com obesidade candidatos à cirurgia bariátrica: análises de classes latentes e fatores associados* [tese]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2019.

Antecedentes: A obesidade e os transtornos mentais são grandes desafios da medicina. A obesidade tornou-se uma epidemia mundial e os transtornos mentais têm sido cada vez mais diagnosticados. Estudos recentes mostraram frequências elevadas de transtornos mentais em pacientes candidatos à cirurgia bariátrica. Este cenário sugeriu que os transtornos psiquiátricos podem ser persistentes, coocorrentes e que haja uma possível formação de agrupamentos de sintomas psicopatológicos entre esses pacientes. **Objetivo:** O objetivo deste trabalho foi: 1) investigar a persistência e a coocorrência dos transtornos psiquiátricos em pacientes com obesidade pré-cirúrgicos; 2) identificar subgrupos psicopatológicos, clinicamente distintos e diferenciados por gêneros, em uma amostra de pacientes com obesidade candidatos à cirurgia bariátrica.

Método: O estudo teve como base a dissertação “Frequência de transtornos mentais entre pacientes obesos candidatos a cirurgia bariátrica, por meio de entrevista clínica estruturada para transtornos do DSM (SCID-I/P)”, apresentada ao programa de pós graduação da Faculdade de Medicina da Universidade de São Paulo. Estudo observacional transversal em pacientes com obesidade grau III que aguardavam a cirurgia bariátrica, no Hospital das Clínicas de São Paulo. Os sujeitos foram recrutados consecutivamente da lista de espera do Ambulatório de Cirurgia Bariátrica – HC-FMUSP e submetidos à entrevista semiestruturada para diagnóstico psiquiátrico: *Structured Clinical Interview for DSM-IV Axis I Diagnosis* (SCID I/P). O tamanho da amostra foi de 393 pacientes; composta por 79,1% de mulheres; média de idade 43 anos e média de IMC: 47,8 kg/m². O curso dos transtornos psiquiátricos foi analisado pela persistência, por meio de razão de prevalência (RP): transtornos atuais/transtornos ao longo da vida (1M/LT); para as comorbidades utilizou-se a análise de correlação tetracórica. Os possíveis agrupamentos psicopatológicos, foram detectados pelo método da análise de classes latentes, baseado na ocorrência de transtornos mentais ao longo da vida, diferenciados por gênero. Análise de regressão logística mostrou a

influência de fatores sociodemográficos na formação das classes psicopatológicas.

Resultados: A maior parte da amostra apresentou dois ou mais transtornos psiquiátricos concomitantes ao longo da vida. Os transtornos de ansiedade foram as condições mais persistentes (a maior razão de prevalência entre transtornos atuais e/ou ao longo da vida) e correlacionaram-se significativamente com transtornos bipolares, depressivos e alimentares. Os transtornos bipolares foram os mais coocorrentes, associaram-se ao uso de substâncias, transtornos alimentares e de ansiedade. Em relação à análise de classe latente, para ambos os sexos, foram detectados três agrupamentos psicopatológicos. Entre as mulheres, as classes latentes foram: (1) “oligossintomático”: 42% das pacientes apresentaram baixa probabilidade de transtornos psiquiátricos; (2) “bipolar com comorbidades”, em 33%; e (3) “ansiedade/depressão”, com 25%. Entre os homens: (1) “bipolar com comorbidades” foi encontrado em 47% dos pacientes; (2) “oligossintomático”, com 40%; e (3) “ansiedade/depressão”, com 13%. Para ambos os sexos, a probabilidade de apresentar transtornos alimentares foi maior nas classes “bipolar com comorbidades” e “ansiedade/depressão”. Transtornos por uso de substâncias foram proeminentes entre os homens “bipolares”. Em comparação com a classe “oligossintomática”, a probabilidade de maior IMC foi observada entre os homens “bipolares” e pior desempenho no trabalho entre os homens com “ansiedade/depressão”. **Conclusões:** Transtornos psiquiátricos são condições frequentes e duradouras entre pacientes à procura de cirurgia bariátrica. Transtornos de ansiedade, humor e alimentares são características persistentes e concomitantes em pacientes em busca de tratamento para obesidade. Homens e mulheres com obesidade grave, pré-cirúrgicos foram distribuídos em três perfis de comorbidades e revelaram padrões psicopatológicos análogos. A classe “bipolar com comorbidades” apresentou coocorrência com transtornos alimentares e uso de substâncias. Esses agrupamentos naturais de transtornos psiquiátricos entre pacientes bariátricos sugerem abordagens terapêuticas específicas e diferenciadas por gênero durante todo o percurso do procedimento cirúrgico.

Descritores: obesidade; cirurgia bariátrica; transtornos mentais; psicopatologia; análise de classe latente; comorbidade.

ABSTRACT

Guerra LSD. *Psychopathological profile of patients with obesity candidate to bariatric surgery: latent class analysis and associated factors*. [Thesis] São Paulo: “Faculdade de Medicina. Universidade de Sao Paulo”; 2019.

Background: Obesity and mental disorders have become major challenges to medicine. Obesity gained worldwide epidemic proportions and the mental disorder has been increasingly diagnosed. Recent study indicated high frequency of mental disorders in patients candidates to bariatric surgery, this panorama suggests that psychiatric disorders can be persistent and co-occurring. These conditions indicates the possibility of subgroups psychopathological between obese patients seeking to bariatric surgery.

Objective: The objective of this study is: 1) to investigate the persistence and co-occurrence, of psychiatric disorders and, 2) identify clinically distinct psychopathological subgroups among a sample of obese patients candidates for bariatric surgery.

Method: The study is based on a study “Frequency of mental disorders among obese candidates for bariatric surgery, using a structured clinical interview for DSM Disorders (SCID-I/P)” presented to the post-graduate program of the Department and Institute of Psychiatry – University of São Paulo. This is a cross-sectional observational study in patients with obesity level III, awaiting bariatric surgery at the Hospital das Clínicas de São Paulo. The subjects were submitted to semi-structured interview for psychiatric diagnosis: Structured Clinical Interview for DSM-IV Axis I Diagnosis (SCID). Were consecutively recruited from the waiting list of the Bariatric Surgery Clinic–HCFMUSP. The sample size was 393 patients 79.1% women; age mean 43 years and mean of BMI 47,8% kg/m². The persistence of group of disorders was defined by prevalence ratio (PR) to denote the one month-to-lifetime (1M/LT). The co-occurrence of psychiatric disorders was investigated by the tetracoric correlation analysis. The possible psychopathological profiles were detected by the method of latent class analysis, based on the occurrence of lifetime psychiatric disorders, differentiated by gender. Logistic regression analysis showed the influence of socio-demographic factors on the formation of psychopathological classes. **Results:** Most of the sample presented two or more co-occurrence lifetime psychiatric disorders. While mood and eating

disorders were frequent conditions, anxiety disorders were the most persistent conditions (the highest one month-to-lifetime prevalence ratio) and were significantly correlated with bipolar, depressive and eating disorders. In relation the latent class analysis, for both genders, the 3-class psychopathological clustering was the best-fitting solution. Among women, the latent classes were: (1) “oligosymptomatic”, where in 42% of patients showed low probability of psychiatric disorders; (2) “bipolar with comorbidities”, in 33%; and (3) “anxiety/depression”, in 25%. Among men, (1) “bipolar with comorbidities” was found in 47% of patients; (2) “oligosymptomatic”, in 40%; and (3) “anxiety/depression”, in 13%. For both genders, the likelihood of eating disorders was higher in both “bipolar with comorbidities” and “anxiety/depression” classes. Substance use disorders was prominent among “bipolar” men. In comparison with “oligosymptomatic” class, the likelihood of higher BMI was observed among “bipolar” men and poorer work attainment among men with “anxiety/depression”. **Conclusion:** Psychiatric disorders are frequent and enduring conditions among patients looking for bariatric surgery. Comorbid anxiety, mood, and eating disorders are remarkable features in treatment-seeking patients with obesity. Three comorbidity profiles were detected in pre-surgical period, in men and women with severe obesity. The class of “bipolar with comorbidities” most likely presented comorbidity with eating and substance use disorder. This natural clustering of psychiatric disorders among bariatric patients suggests gender-related therapeutic approaches.

Keywords: Obesity; bariatric surgery; psychiatric disorders; psychopathology; latent class analyses; comorbidity.

1-Introdução

Atualmente, os transtornos psiquiátricos e a obesidade são considerados grandes desafios para a saúde mundial. Segundo as projeções da Organização Mundial de Saúde para o século XXI, as doenças não transmissíveis (DNT) serão responsáveis pelas maiores cargas das doenças no globo.^{1,2} Os transtornos neuropsiquiátricos, ao lado das doenças cardiovasculares e respiratórias, destacam-se como o principal grupo de agravos de saúde entre as DNT, sendo responsáveis por quase um terço das incapacitações de saúde.³

Publicações recentes apontam que a maioria das cargas de doenças neuropsiquiátricas no Brasil foi atribuída a transtornos psiquiátricos como depressão, psicoses e transtornos associados ao uso nocivo do álcool.³ Dados brasileiros do estudo *World Health Survey*⁴, concluído em 2003, com metodologia padronizada internacional, mostraram que 18,8% dos brasileiros relataram ter recebido um diagnóstico de depressão nos últimos 12 meses. Recentemente, em pesquisa realizada na região metropolitana de São Paulo, a prevalência de depressão, no último mês, foi de 9,2%,⁵ considerada uma das maiores taxas ao redor do mundo quando comparada com outros estudos.⁶

Assim como os transtornos psiquiátricos, a obesidade também atinge índices alarmantes. Segundo dados recentes da Organização Mundial de Saúde (OMS), 12% da população mundial, cerca de 800 milhões, tem obesidade e 35% apresentam sobrepeso.⁴ No Brasil, há cerca de 30 milhões de pessoas com obesidade, o que representa 18% da população adulta brasileira⁴, sendo que 3% tem obesidade grau III, com índices de massa corporal (IMC) ≥ 40 .⁷

A associação entre a obesidade e os transtornos mentais vem sendo destacada pela literatura internacional, em que os transtornos psiquiátricos são condições frequentes entre pessoas com obesidade.⁸⁻¹⁰ Na população geral, a obesidade e os transtornos psiquiátricos afetam cerca de 12% e 30% dos indivíduos adultos, respectivamente.¹¹⁻¹⁴ Na população geral dos EUA com obesidade, há cerca de 25% de aumento nas chances de transtornos de humor e ansiedade e 25% de diminuição nas chances de transtornos por uso de substâncias.⁸ Portanto, compreender a associação entre obesidade e transtornos psiquiátricos implica redução da carga clínica dessas patologias em termos de etiologia e terapêutica.

De acordo com uma recente meta-análise, os transtornos da compulsão alimentar

(TCA) e a depressão são os distúrbios isolados mais frequentes em indivíduos com obesidade que são submetidos a cirurgia de redução de peso, observados em, respectivamente 17% e 19% das amostras.¹⁵ A cirurgia bariátrica se popularizou como um efetivo procedimento para diminuição e manutenção de peso, entre pacientes com elevados IMC. Entre pacientes candidatos a cirurgia bariátrica de 36% a 89% deles, preenchem algum critério para transtornos psiquiátricos.¹⁵⁻²¹

A associação dos transtornos psiquiátricos e obesidade não é um tema recente, porém, a complexa associação dessas patologias, apesar de muito investigada, ainda deixa lacunas a serem preenchidas. Um desses espaços inexplorados está relacionado com o fato de que os estudos existentes desprezam o curso e a concomitância dos transtornos psiquiátricos entre pacientes com obesidade grau III, e abordam os transtornos de forma única. Por sua vez, a análise do cenário que circunda o procedimento cirúrgico e a multidisciplinariedade envolvida, tanto no pré como pós operatório, mostra que poucos profissionais de saúde estão cientes da frequente comorbidade dos transtornos depressivos, bipolares, ansiosos, alimentares e de uso de substâncias em populações com obesidade.²²

Estudos do percurso e padrões de comorbidade psiquiátricas em pacientes com obesidade no pré-operatório são raros e pouco conclusivos, no entanto, a literatura aponta que cerca de dois terços dos pacientes que procuram cirurgia bariátrica apresentam dois ou mais transtornos psiquiátricos concomitantes.^{23,24} Portanto, a comorbidade psicopatológica parece ser mais regra que exceção entre os pacientes bariátricos.

Análises primárias do estudo “Frequência de transtornos mentais em pacientes obesos candidatos à cirurgia bariátrica por meio de Entrevista Clínica Estruturada para Transtornos do DSM (SCID-I/P)”, mostraram frequências elevadas de transtornos psiquiátricos entre pacientes candidatos à cirurgia bariátrica, sugerindo que o transtorno mental, entre pacientes com obesidade, apresentava-se com um curso e forma singular. Deste modo, este será o estudo base utilizado para esta tese. Esta dissertação foi apresentada à Faculdade de Medicina da Universidade de São Paulo para obtenção do título de Mestre em Ciências, que originou o artigo “*Psychiatric disorders among obese patients seeking bariatric surgery: results of Structured Clinical Interviews*”, publicado na revista “*Obesity Surgery*”, Vol. 24, p. 11. (Apêndice).

A partir dos resultados primários do estudo base, deu-se continuidade a uma etapa de análises secundárias dos dados. Primeiro, investigamos o curso e a coocorrência das morbidades psiquiátricas em pacientes candidatos à cirurgia bariátrica, por meio do cálculo da persistência dos transtornos psiquiátricos e do coeficiente de correlação tetracórica, respectivamente. Os resultados dessas análises, por sua vez, conduziram a uma nova investigação, cujo objetivo foi identificar possíveis padrões psicopatológicos, ou subgrupos de pacientes com obesidade aglomerados por critérios psicopatológicos. Para esta análise foi utilizado o método estatístico, análise de classes latentes (ACL).

Os resultados dessas investigações foram apresentados em dois artigos. O primeiro artigo “*Morbidity persistence and comorbidity of mood, anxiety, and eating disorders among preoperative bariatric patients*”, publicado na ***Psychiatric Research***; 2017 Nov; 257:1-6, apresenta o curso e a coocorrência dos transtornos psiquiátricos e discussão da importância do fluxo das comorbidades no procedimento cirúrgico, que envolve tanto o período pré como pós cirúrgico. O segundo artigo “*Gender-related patterns of psychiatric disorder clustering among bariatric surgery candidates: a latent class analysis*”, publicado no ***Journal Affective Disorders***; (2018) 240: 72-78, traz os padrões de comorbidades psicopatológicas entre pacientes pré-cirúrgicos, separados por gêneros, além de mostrar fatores que influenciaram esse agrupamento.

A análise por gênero tem por justificativa o fato de homens e mulheres serem afetados em diferentes proporções por transtornos alimentares (TA). Homens têm IMC mais elevados e quadro mais grave de transtornos psiquiátricos, como a mania e uso de substâncias.²⁴⁻²⁶ A conexão entre obesidade, transtornos psiquiátricos e gênero ainda não foi devidamente investigada, bem como se fatores sociodemográficos influenciam essa correlação. Particularidades entre homens e mulheres com obesidade é pouco compreendida em contextos bariátricos e o presente estudo poderá favorecer a atendimentos diferenciados ao longo do procedimento cirúrgico bariátrico.

A análise do curso e coocorrência das comorbidades, bem como a identificação dos perfis psicopatológicos, contribuirá, ainda, com toda a engrenagem multidisciplinar que envolve a trajetória do tratamento do paciente bariátrico. Novas intervenções e medidas preventivas, poderão elevar a possibilidade de bons prognósticos, bem como a introdução de estratégias de saúde pública, tanto no campo da cirurgia bariátrica, como em tratamentos não cirúrgicos.

2- Revisão de Literatura

2.1. Obesidade

A obesidade é uma das mais importantes enfermidades metabólicas do mundo ocidental²⁷, sendo responsável por cerca de dois terços da carga global de doenças atribuídas à doença crônica segundo a projeção da OMS.⁴ Entretanto, os países da América Latina apresentam um cenário paradoxal, uma vez que neles os estados de desnutrição coexistem com a obesidade.²⁸

Em 1869, Quetelet²⁹ descreveu uma fórmula para calcular o índice de massa corpórea (IMC) presumindo a quantidade de gordura corporal de acordo com o peso (em quilograma) e corrigido para a altura (em metros). Modernamente, a mensuração da obesidade se faz por medidas antropométricas (peso e altura), pelas pregas cutâneas (*skinfold*), pela impedância bioelétrica e pelo índice de massa corporal (IMC). A existência de um método quantitativo simples de mensuração da superfície corporal, com ampla aceitação internacional, permitiu comparações longitudinais com boa reprodutibilidade dos resultados. A *International Obesity Task Force* (<http://www.iaso.org/iotf/>) categorizou o índice de massa corpórea de acordo com o peso ideal esperado para indivíduo e risco para doença. De acordo com este critério, pessoas com IMC entre 30,0 – 34,9 kg/m² (classe I) apresentam riscos moderados para surgimento de doenças clínicas; IMC 35,0 - 39,9 kg/m² (classe II) apresentam riscos graves de doenças clínicas concomitante e IMC > 40 kg/m² (classe III) constituem um grupo de indivíduos com risco elevado para doenças clínicas comórbidas. Na maioria das vezes, o indivíduo com obesidade da classe III apresentam um excesso de mais de 40% de seu peso ideal. Alguns autores, entretanto, definem a obesidade classe III como um excesso de peso igual ou superior a 45 kg ou mais, baseado no peso esperado para idade, sexo e altura, de acordo com a tabela de peso corporal ideal definido pelas tabelas da *Metropolitan Life Insurance Company*.²⁹

Os modelos neurobiológicos e psicológicos atuais que definem a obesidade remontam à história da psicopatologia e da biotipologia. O psiquiatra alemão Ernst Kretschmer,³⁰ servindo-se da inspeção morfológica externa (ectoscopia), medidas de antropometria e outros recursos complementares, descreveu três tipos fundamentais de arquitetura corporal: o leptossômico (astênico, em suas formas extremas), o pícnico e o

atlético. Descreveu, ainda, um quarto grupo heterogêneo que denominou de displásicos especiais. Neste grupo, estariam incluídos indivíduos que lembram determinadas síndromes endócrinas, devido a algumas características típicas.

Na atualidade, as teorias e pesquisas sobre obesidade caminham em duas direções: nos aspectos biológicos e psicológicos. A maioria dos autores modernos vê, no entanto, a obesidade como um modelo prototípico do resultado de uma rede complexa de interações entre: predisposição genética, aspectos neurobiológicos e a escolha do estilo de vida.³¹ No final do século XX, o modelo social de valorização estética de um corpo magro e alimentação saudável, repercute na compreensão daqueles indivíduos com excesso de peso. A obesidade ganhou dimensões de uma grave condição clínica no século XXI, sendo vista como um problema de saúde pública de amplitude preocupante.⁴ A obesidade classe III ($\text{IMC} \geq 40 \text{ kg/m}^2$), resiste aos métodos habituais de redução de peso; os indivíduos com obesidade seguem numa progressão de ganho de peso que os tornam incapacitados, com dificuldade de locomoção, clinicamente disfuncionais e com um corpo humano disforme. A morte subsequente é uma consequência de uma evolução desfavorável das doenças cardiovasculares.

Segundo as projeções da Organização Mundial de Saúde⁴, o Brasil será em 2025 o 5º país do mundo a apresentar mais problemas de obesidade.³² No Brasil, a prevalência dessa condição aumentou em 70% entre 1975 e 1989, indicando que o excesso alimentar está se expandindo mais rapidamente do que a deficiência nutricional.³³ Adicionalmente, a obesidade triplicou nos últimos 30 anos em crianças e adolescentes nas investigações seriadas sobre o peso da população brasileira.³⁴ Levantamentos realizados pela Vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico (Vigitel), desde meados dos anos 70 até 2017, mostraram um aumento substancial da frequência de sobrepeso, diferenciados por faixa etária, gênero e nível socioeconômico. Segundo os últimos levantamentos, há uma estabilização no crescimento, permanecendo no patamar de aproximadamente 18% da população com obesidade.³⁵⁻³⁹

2.2 Doenças neuropsiquiátricas e obesidade

A literatura internacional aponta a associação entre a obesidade e os transtornos mentais.^{40,41} Estudos clínicos e biológicos sugerem existir grande semelhança entre os transtornos alimentares e os transtornos do humor.^{42,43} A exata relação entre obesidade e transtornos neuropsiquiátricos é inconclusiva, alguns pesquisadores argumentam que a utilização de medicamentos neuropsiquiátricos pode ser responsável pelo ganho de peso observado nestes pacientes.⁴⁰ A controvérsia aumenta quando se discute a direção de causalidade, pois a simples relação bidirecional parece ser mais complexa do que se imaginava. Quadros psiquiátricos podem ser pré-existentes, precipitados ou intensificados após uso de medicamentos ou drástico emagrecimento por meio de intervenção cirúrgica.²⁹

A associação entre obesidade e transtorno mental, bem como a compreensão sobre a inter-relação, permanece um debate inacabado.^{17,44,45} Na população adulta americana, a obesidade está associada com aumento de 25% nas chances do indivíduo ter um transtorno de humor ou de ansiedade.⁸ Os autores ponderam que fatores socioculturais poderiam moderar ou mediar a associação entre obesidade e transtornos de humor. Dentre os transtornos de humor, o transtorno bipolar (TB) destaca-se entre as pesquisas; estudos investigam a correlação de sintomas de mania e hipomania com obesidade.⁴⁶⁻⁴⁹

O tratamento da obesidade, especificamente da obesidade classe III, mostra que a obesidade em estágios avançados, apresenta uma resposta pobre às intervenções terapêuticas não invasivas, como dieta restritivas, recomendação de mudança de estilo de vida (aumento de atividade física, psicoterapias) e prescrição de fármacos. Muitas vezes, intervenções mais agressivas, como a gastroplastia,⁵⁰ são necessárias para combater os efeitos adversos da obesidade e a sua progressão desfavorável para doenças crônicas metabólicas e cardiovasculares.

A técnica cirúrgica para o tratamento de obesidade foi proposta, pela primeira vez, em 1954, por Kremen, com a diminuição do intestino, reduzindo a capacidade absorviva.⁵¹ São candidatos para o tratamento cirúrgico (cirurgia bariátrica) os pacientes com IMC maior que 40 kg/m² ou com IMC maior que 35 kg/m² associado a comorbidades clínicas: hipertensão arterial, dislipidemia, diabetes tipo 2, apneia do sono, entre outras. O Brasil aparece em 2º lugar em número de cirurgias realizadas, só

perdendo para os Estados Unidos, com predomínio da técnica de *Bypass gástrico*. A eficácia e efetividade da cirurgia no controle de peso e na melhora na qualidade de vida da maioria dos pacientes foram documentadas em diversos estudos.⁵²⁻⁵⁶

Apesar da eficácia do procedimento cirúrgico, vários estudos⁵⁷⁻⁵⁹ apontam que, após dois anos da cirurgia, alguns pacientes passam a apresentar transtornos psiquiátricos como: transtornos do humor (depressão e transtornos bipolares), transtornos alimentares (anorexia, bulimia e compulsão), ansiedade e uso de substâncias.^{8,57,60-62} O estudo americano de Simon e colaboradores apontou que as pessoas obesas têm 25% mais probabilidade de apresentar transtornos psiquiátricos.⁸ Assim, torna-se recomendável o acompanhamento psiquiátrico de pacientes submetidos à cirurgia bariátrica em todos os estágios do procedimento. A cirurgia bariátrica traz transformações psíquicas, sociais e físicas e os profissionais da área de saúde mental devem estar instrumentalizados para compreender e atuar, tanto antes quanto após a cirurgia.⁶³

Revisando a literatura sobre o tema, a Tabela 2 resume pesquisas já realizadas sobre transtornos mentais entre pacientes com obesidade grave em amostras clínicas.

Tabela 1 - Frequência de transtornos mentais diagnosticados por meio de entrevista clínica padronizada semiestruturada (SCID-I/P) entre pacientes com obesidade classe III.

Autor (ano)	País	N	% Mulheres	IMC	Diagnóstico atual	Diagnóstico em vida
Rosenberg e cols. (2006) ⁴⁶	Estados Unidos	174	75,3	50,2	24,1%	36,8%
Alciati e cols. (2007) ⁴⁵	Itália	86	76,5	42,5	--	89,0 %*
Kalarchian e cols. (2007) ¹⁷	Estados Unidos	288	83,3	52,2	37,8%	66,3%
Mauri e cols. (2008) ²¹	Itália	282	79,8	> 40	22,0%	38,0%
Mühlhans e cols. (2009) ¹⁸	Alemanha	146	71,9	49,3	55,5%	72,6%
Mitchell e cols. (2012) ²⁴	EUA	199	82,9	44,9	33,7%	68,8%
Lin e cols. (2013) ¹⁹	China	455	72,1	35,2	--	54,1%
Duarte-Guerra e col. (2015) ¹⁶	Brasil	393	79,1	47,8	57,8%	80,9%

N: tamanho da amostra; IMC: média de índice de massa corpórea em kg/m²

SCID-I/P: *Structured Clinical Interview for Axis-I Diagnosis of DSM-IV*;

* Diagnóstico de transtornos do espectro bipolar

Apresentaremos os principais resultados da estudo brasileiro “Frequência de transtornos mentais em pacientes obesos candidatos à cirurgia bariátrica por meio de entrevista estruturada para transtornos do DSM-IV (SCID-I/P)”, que foi o estudo base para esta tese de doutorado. Nesse estudo, os dados mostram que a frequência de algum transtorno mental ao longo da vida foi de 80,9% (81,7% homens e 80,7% mulheres). A taxa de frequência de transtornos mentais no momento da entrevista foi 57,8% (58,5% homens e 57,6% mulheres). Os transtornos afetivos foram os mais frequentes (64,9%), sendo os transtornos bipolares e os transtornos depressivos os mais comuns (35,6% e 29,3%). Entre os entrevistados que apresentaram quaisquer transtornos mentais ao longo da vida, cerca de metade da amostra apresentou três ou mais transtornos simultâneos. Os transtornos de ansiedade foram os diagnósticos mais frequentes (46,3%) entre os participantes com transtorno atual. Idade e nível educacional estão associados com a probabilidade de apresentar transtornos mentais no momento da entrevista.

2.3. Curso e comorbidade dos transtornos psiquiátricos em obesidade

Pesquisas usando critérios diagnósticos do DSM-IV relatam que entre 36,8% e 80,9% dos pacientes com obesidade candidatos à cirurgia bariátrica apresentam algum transtorno psiquiátrico ao longo da vida.¹⁵⁻²¹ No entanto, o impacto da frequência elevada de transtornos psiquiátricos em todas as etapas do processo cirúrgico é pouco compreendida. De acordo com meta-análise recente, o transtorno da compulsão alimentar e depressão são os transtornos isolados mais frequentes em candidatos à cirurgia de redução de peso, observadas, respectivamente, em 17% e 19% das amostras.¹⁵ Casos ativos de transtornos psiquiátricos podem adiar ou barrar a indicação à cirurgia. A evolução dos transtornos psiquiátricos, bem como o padrão de fenótipos de comorbidades em pacientes bariátricos, podem influenciar no processo de perda e manutenção de peso, bem como na recuperação pós-cirúrgica com piora de qualidade de vida no período de acompanhamento.

Apesar do conhecimento sobre associação frequente entre transtornos psiquiátricos e obesidade grave em amostras bariátricas, o padrão de curso e comorbidade de transtornos psiquiátricos são raramente investigado em pacientes com obesidade mórbida. O curso dos transtornos pode ser avaliado por sua persistência, porém na literatura há pouco consenso sobre a definição de persistência da doença.⁶⁴ A incerteza sobre a idade de início da doença levou alguns estudiosos a focarem na duração do tratamento como indicador de incapacitação e prognóstico. Embora o monitoramento contínuo do diagnóstico de um paciente seja inquestionável, padrões específicos de doença, etnia e fatores culturais podem interferir na duração de uma doença.⁶⁵

A persistência de um determinado transtorno é frequentemente associada ao grau de gravidade da doença; por exemplo, a persistência de psicopatologia entre candidatos à cirurgia bariátrica pode influenciar o desfecho em relação à perda de peso e à qualidade de vida no período pós-operatório.⁶⁶ Deste modo, a abordagem tradicional para documentar a persistência de doenças é estimada pelos riscos de morbidade ao longo da vida por meio de análise de sobrevivência.⁶⁷ Abordagem alternativa analisou a persistência da doença, como a razão de duração de casos recorrentes ao longo da vida.⁶⁸ Comparando com a população geral, pacientes com doenças psiquiátricas crônicas tem mais chances de terem obesidade,⁶⁹ porém o padrão de persistência dos transtornos psiquiátricos nessa população ainda é subpesquisado.

Em relação à coocorrência dos transtornos psiquiátricos, pacientes com duas ou mais condições psiquiátricas, estão associados à inadequação de tratamento e a desfechos desfavoráveis de perda de peso, quando comparados com aqueles que apresentam um transtorno único.⁷⁰ Padrões de comorbidade podem prever perda de peso e qualidade de vida em todas as fases da cirurgia bariátrica, com implicações clínicas no resultado cirúrgico.^{70,71}

A comorbidade psicopatológica parece ser mais regra do que exceção entre pacientes bariátricos. A influência dos transtornos psiquiátricos em todas as fases da cirurgia bariátrica só pode ser vislumbrada quando o padrão de comorbidade é considerado. No entanto, observa-se que a maioria dos estudos investigou a frequência do transtorno psiquiátrico de forma única, tanto no pré-operatório quanto período pós-

cirúrgico, porém dois terços dos pacientes que procuram cirurgia bariátrica apresentam dois ou mais transtornos psiquiátricos concomitantes.^{23,24} Transtornos depressivos, bipolar, ansiedade, alimentação e transtornos por uso de substâncias estão correlacionados, porém poucos profissionais de saúde estão cientes destas comorbidades em população com obesidade.²²

Padrões de comorbidade diferenciados por gêneros foram pesquisados na população geral.^{26,60} Um grande estudo comunitário do *National Epidemiological Study of Alcohol and Related Conditions* (NESARC) encontrou associação entre obesidade (IMC > 30), transtornos depressivos e ansiosos em ambos os sexos.⁷² Do mesmo modo, os transtornos alimentares parecem afetar os homens e mulheres com obesidade em proporção comparável.^{25,26,73} Em relação ao transtorno bipolar, a maioria dos estudos indica que as mulheres apresentam maior risco de obesidade que os homens.^{60,72} Contudo, a obesidade está associada ao aumento de risco de uso de álcool em homens ao longo da vida.⁷⁴

A conexão entre obesidade, transtornos mentais e diferenças de gênero é pouco compreendida entre as equipes multidisciplinares do procedimento bariátrico. Como tal, as investigações sobre padrão de comorbidade em amostras clínicas de pacientes com obesidade, diferenciadas por gênero, torna-se imprescindível. Poucos estudos analisaram o curso e os padrões de comorbidade em pacientes com obesidade no período pré-operatório. Transtornos pré-existent não diagnosticados na avaliação pré-operatória podem permanecer ou até mesmo se intensificar após a cirurgia, bem como novas formas de psicopatologia podem ocorrer durante o processo. Esta instabilidade mutável dos transtornos psiquiátricos pode afetar o sucesso do procedimento de redução de peso.

2.4. Subgrupos de apresentação psicopatológica em obesidade

A maioria das pesquisas científicas trabalha com variáveis observáveis, no entanto, em algumas áreas é bastante comum o interesse por variáveis que não se manifestem de maneira direta. Essas variáveis não observáveis diretamente são denominadas variáveis latentes e são estimadas e exploradas a partir das observáveis.

Assim como as variáveis observáveis, as variáveis latentes podem ser quantitativas ou categóricas (nominais ou ordinais).

Há várias técnicas apropriadas para agrupar as variáveis observáveis em perfis distintos. A análise de classes latentes (ACL) é um método estatístico utilizado para identificar construtos subjacentes que expliquem as relações de interdependência entre indicadores observados. Como os construtos teóricos não podem ser diretamente observados, a mensuração pode ser obtida por meio de um ou mais indicadores observáveis (por ex.: itens de questionários, comportamentos, sintomas). Os indicadores observados servem como instrumento de mensuração para os construtos e também são chamados de variáveis latentes. As variáveis latentes podem ser categóricas ou dicotômicas em relação as dimensões latentes identificadas.

Considerada uma variante da análise fatorial, o modelo de classes latentes vai além e possui vantagens em relação a esta: reduz a dimensionalidade dos dados observados e amplia as observações em relação às dimensões latentes identificadas; estabelece de forma objetiva o número ideal de classes, comparando estatisticamente os ajuste dos melhores modelos; estima a probabilidade de um indivíduo pertencer a cada uma das classes; testa a invariância entre grupos; além de ser possível incluir covariáveis que auxiliam a prever a classe latente do indivíduo. Estudos epidemiológicos têm feito amplo uso desse recurso.⁷⁵

Os precursores desse tipo de análise vieram das Ciências Sociais⁷⁶ e de um estudo do comportamento com dados da segunda guerra mundial.⁷⁷ Segundo Goodman (2002)⁷⁸ esses modelos, usados como ferramenta para auxiliar a compreender a relação entre variáveis categóricas observadas, avançaram na segunda metade do século XX. Embora no início do século XIX alguns modelos matemáticos, considerados casos especiais dos modelos de classes latentes, já fossem utilizados. As áreas de aplicação dos modelos de classes latentes são diversas, sendo empregados principalmente em estudos que visam a identificar comportamentos, percepção e outros traços psicológicos/psiquiátricos.^{79,80}

Estudos na população geral nos EUA, utilizando o método da ACL, apresentaram diferentes padrões sintomáticos de transtornos psiquiátricos. A classe com transtorno bipolar apareceu como sendo a classe mais comórbida e grave.^{11,79} Entre os pacientes com obesidade, o método de ACL explorou fenótipos de transtornos alimentares^{81,82} e traços de temperamento em pacientes pré-bariátricos.⁸³ Entre pacientes candidatos à cirurgia bariátrica, alguns estudos exploraram os padrões psicossomáticos. A ACL foi utilizada em estudo com adolescentes pré-cirúrgicos, e identificou três subgrupos sintomáticos: transtorno alimentar com comorbidade, pouca psicopatologia e psicopatologias não específicas.⁸⁴ Com metodologia similar a ACL, análise de cluster, Martínez e colegas (2013)⁸⁵ também identificaram subgrupos psicopatológicos em adultos pré-cirúrgicos, e o transtorno bipolar foi o que ganhou destaque. A diferença de gênero nos padrões de transtornos psicopatológicos, documentada na população geral, foi influenciada por fatores biológicos e socioocupacionais.^{86,87}

2.5 - Hipóteses

1. Os transtornos mentais em pacientes bariátricos são persistentes e comórbidos. Estudos indicam que cerca de dois terços dos pacientes candidatos à cirurgia bariátrica preenchem critérios para dois ou mais transtornos psiquiátricos concomitantes.²³ No estudo longitudinal LABS-3, os resultados mostraram que os transtornos do humor e ansiedade são os mais frequentes e apresentaram-se associados a transtornos por uso de substâncias.²⁴ Portanto, parece haver um padrão de apresentação psicopatológica entre os pacientes com obesidade grave, com maior cronicidade e presença de múltiplos transtornos psiquiátricos.
2. Há padrões distintos de psicopatologia que se diferenciam entre homens e mulheres candidatos à cirurgia bariátrica. Estudos sobre diferenças de gêneros, associados com o índice de massa corporal, mostram que homens apresentam índices mais elevados e transtornos psiquiátricos mais graves, como mania e uso de substâncias; mulheres por sua vez, são mais depressivas.^{25,26.}

3. Há fatores sociodemográficos que influenciam os agrupamentos dos transtornos psiquiátricos. No estudo de frequências de transtornos psiquiátricos entre pacientes candidatos a cirurgia bariátrica, foi realizada uma logística multinomial e os resultados da regressão mostraram que idade e anos de estudos são significantes como fatores associados (ou correlacionados) à probabilidade dos participantes apresentarem transtornos psiquiátricos.¹⁶

2.6 - Objetivos

1. Investigar o curso dos transtornos psiquiátricos e a coocorrência de morbidade psiquiátricas em pacientes candidatos à cirurgia bariátrica.
2. Identificar subgrupos de pacientes com perfis psicopatológicos homogêneos em termos de transtornos psiquiátricos concomitantes, diferenciados por gênero.
3. Verificar se fatores associados, como sexo, IMC, idade, ocupação e escolaridade podem influenciar nas características de subgrupos de pacientes com obesidade.

3 - Método e Casuística

3.1 Tipo de estudo

O presente estudo tem como base o estudo transversal “Frequência de transtornos mentais em pacientes obesos candidatos à cirurgia bariátrica por meio de entrevista estruturada para transtornos do DSM-IV (SCID-I/P)”. Dissertação apresentada à Faculdade de Medicina da Universidade de São Paulo para obtenção do título de Mestre em Ciências, aprovada pelo Comitê de Ética do Hospital das Clínicas da Faculdade de Medicina de São Paulo-FMUSP, protocolo 0228/11 (Anexo I) e anuência de pesquisa interdepartamental do Departamento de Gastroenterologia FMUSP (Anexo II). Contou com o apoio da Fundação de amparo à pesquisa do Estado de São Paulo – FAPESP, processos 2012/17435-7 e 2012/17498-9.

3.2. Delineamento do Estudo “Frequência de transtornos mentais em pacientes obesos candidatos à cirurgia bariátrica por meio de entrevista estruturada para transtornos do DSM-IV (SCID-I/P)” (Estudo base)

O estudo “Frequência de transtornos mentais em pacientes obesos candidatos à cirurgia bariátrica por meio de entrevista estruturada para transtornos do DSM-IV (SCID-I/P)” é uma pesquisa transversal observacional de fase única, no qual foi levantada a frequência de transtornos mentais em pacientes com obesidade candidatos à cirurgia bariátrica. O estudo levantou as frequências dos transtornos segundo critérios do DSM-IV. Os resultados estão apresentados em tabelas com as frequências e desvio padrão, separados por gênero. Dados demográficos foram avaliados por regressão logística e verificou-se que idade, escolaridade e análise de desempenho global (*GAF-Global Assessment of Functioning*) são fatores associados à ocorrência de transtornos mentais. Esta pesquisa foi realizada como dissertação de mestrado apresentada ao programa de pós-graduação do Departamento de Psiquiatria, realizada por Leorides Severo Duarte Guerra, tendo como orientador Dr. Wang Yuan Pang.

3.2.1 Sujeitos da amostra do Estudo base

Os pacientes candidatos à gastroplastia foram recrutados na Clínica de Gastroenterologia, no Ambulatório de Cirurgia Bariátrica do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HC-FMUSP). Este Ambulatório é um serviço universitário terciário que fornece avaliação médica, procedimento cirúrgico e seguimento clínico aos pacientes com obesidade grave de várias regiões brasileiras. No período da coleta dos dados, anualmente, cerca de 1.200 pacientes procuraram o Programa de Cirurgia Bariátrica por obesidade grave ou consequências decorrentes do excesso de peso. Todos os participantes assinaram o Termo de Consentimento Livre e Esclarecido. (Anexo III)

Para serem incluídos no Programa da Cirurgia Bariátrica do HC-FMUSP, os pacientes deveriam apresentar as seguintes características:

- (a) Apresentar IMC maior ou igual a 40 (ou ≥ 35 com comorbidades);
- (b) Frequentar a palestra educacional sobre procedimentos cirúrgicos para conhecerem os riscos e benefícios da gastroplastia.

Pacientes com graves transtornos mentais, como psicoses e retardo mental, eram excluídos do programa. Os pacientes elegíveis eram matriculados no Programa de Cirurgia Bariátrica, com abertura de um prontuário médico e subsequente solicitação de exames clínicos de avaliação pré-cirúrgica. Durante este período pré-cirúrgico, os pacientes eram avaliados por meio de exames clínicos, recebiam assistência psicológica e orientação nutricional. Este serviço admitia cerca de 500 novos pacientes num período de 12 meses. O tempo médio entre a admissão e o procedimento cirúrgico era de cerca de 60 meses. A lista de espera dos candidatos à cirurgia bariátrica era ordenada de acordo com a anterioridade de inclusão no Programa e a gravidade do quadro clínico (por ex.: a presença de comorbidades médicas e risco de vida). No período da coleta, estimava-se que essa lista acumulava um número de, aproximadamente, 5.000 pacientes aguardando o procedimento cirúrgico.

A amostra do estudo base incluiu pacientes regularmente matriculados no Programa de Cirurgia Bariátrica do HC-FMUSP, e que também preencheram os seguintes critérios adicionais da pesquisa:

- (1) Indivíduos adultos (idade acima de 18 anos);
- (2) Capazes de ler, compreender e assinar o termo de consentimento livre e esclarecido.

Os critérios de exclusão da pesquisa base foram:

- (1) Pacientes submetidos à cirurgia bariátrica anterior, independentemente do tempo decorrido da primeira cirurgia, mas que estão aguardando nova operação para corrigir as complicações pós-cirúrgicas;
- (2) Incapazes de completar as avaliações por dificuldade linguística, de mobilidade, baixa escolaridade que incapacite ler e assinar o termo de consentimento, residir em local distante sem possibilidade de comparecer às avaliações agendadas.

Para o cálculo do tamanho da amostra⁸⁸ levou-se em conta a frequência de transtorno mental em pacientes que aguardavam cirurgia bariátrica (de 89% segundo Alciati e colaboradores⁴⁵, e admitindo um erro amostral de 5%). O cálculo do tamanho amostral foi realizado sob o número de 500 pacientes, que aderem ao programa anualmente. Foi realizado por meio da calculadora eletrônica disponível no site do Laboratório de Epidemiologia e Estatística Lee-Dante⁸⁹ data de acesso: 19 de março de 2010.

3.2.2 Instrumento de avaliação padronizada do Estudo base

As seguintes informações foram coletadas para todos os participantes:

- a) Variáveis sociodemográficas. Foi utilizado questionário clínico que colheu dados de identificação e características sociodemográficas dos participantes do estudo, como nome (iniciais), idade, estado civil, escolaridade, uso de

tabaco, histórico de obesidade na família, ocupação atual e antecedentes de transtorno psiquiátrico e/ou psicológico (Anexo IV);

- b) *Structured Clinical Interview for DSM-IV Axis I Diagnosis* (SCID-I/P)⁹⁰– Entrevista Clínica Estruturada para Transtornos do Eixo I do DSM-IV. Trata-se de uma entrevista semiestruturada com os critérios operacionais do DSM-IV, que é amplamente aceita como “padrão-ouro” nas pesquisas de transtornos mentais.⁹¹ Após um rastreamento sobre possíveis transtornos mentais, o entrevistador deverá investigar se o paciente preenche os critérios para algum transtorno. A SCID-I/P é dividida por módulos, sendo: transtornos afetivos (seção A e B), transtornos psicóticos (seção C e D), uso de substâncias (seção E), transtornos de ansiedade (seção F), transtornos somatoformes (seção G), transtornos alimentares (seção H) e transtornos de ajustamento (seção I). A estratégia de diagnóstico adotada pela SCID-I/P é *top-down*, ou seja, o entrevistador deve verificar a presença de sintomas que satisfazem um conjunto de critérios para um determinado diagnóstico psiquiátrico. Nesta pesquisa, utilizou-se a versão para pacientes SCID-I/P, que permite levantar transtornos no momento da entrevista e ao longo da vida. A seção de transtornos psicóticos e transtornos somatoformes não foi avaliada para encurtar o tempo de aplicação e também, porque pacientes com psicoses são excluídos do programa de cirurgia bariátrica (Anexo V).

3.2.3 Procedimentos do Estudo base

3.2.3.1 Recrutamento

Os pacientes matriculados no ambulatório de cirurgia bariátrica e pertencentes à lista de espera foram contatados por telefone para participarem da pesquisa. Foram cinco blocos de cem pacientes. Neste contato inicial, os pacientes receberam uma breve explicação geral sobre os objetivos da pesquisa, e foram convidados para participação voluntária e anônima. Após aceitação, foram agendados dia, horário e local para a aplicação dos questionários.

3.2.3.2 Entrevistadores

Uma equipe de seis psicólogas clínicas recebeu treinamento para se familiarizar com os instrumentos e foram supervisionadas durante a investigação pelo professor orientador. O treinamento dos entrevistadores para a entrevista estruturada SCID-I/P foi oferecido pelo Centro de Treinamento de Entrevistas Diagnósticas do Núcleo de Epidemiologia Psiquiátrica (LIM-23) da FMUSP. Os entrevistadores receberam treinamento de 30 horas. Para análise de confiabilidade interjuízes, os primeiros 15 participantes foram avaliados por pares de entrevistadores. Os entrevistadores eram cegos para a amostra, e os pacientes foram aleatoriamente designados para o primeiro assistente de pesquisa disponível. Uma estagiária de Psicologia (bolsista de iniciação científica associada a esta pesquisa) encaminhou os pacientes convocados para a sala de entrevista.

3.2.3.3 Participantes

Dos 500 pacientes elegíveis da lista de espera, 63 dos contatados se recusaram a participar durante o prévio convite por telefone e 44 foram excluídos após rastreamento. Os motivos de exclusão foram: sintomas prévios de graves transtornos mentais como psicose (um caso), retardo mental (um caso), já ter realizado algum procedimento cirúrgico bariátrico (cinco casos) e dificuldades de locomoção que inviabilizaram o acesso ao ambulatório (37 casos). A amostra final foi composta por 393 pacientes que concluíram a entrevista.

3.2.3.4 Aplicações

O estudo contou com a aplicação da entrevista em um único encontro. A entrevista teve duração entre 60 a 90 minutos, dependendo da complexidade da história psiquiátrica e o padrão de comorbidade.⁹⁰ Todas as entrevistas ocorreram no

Ambulatório de Cirurgia Bariátrica da Clínica de Gastroenterologia do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, localizado na Av. Dr. Enéas de Carvalho Aguiar, 255 – 6º andar. Todas as avaliações foram realizadas entre novembro de 2010 e março de 2012. Os quatro primeiros meses foram de treinamento e aplicações para estabelecer a calibração dos instrumentos entre os pesquisadores e preparação do material a ser utilizado. Finalizadas as aplicações, os dados foram armazenados num banco do programa SPSS. Um membro da equipe de pesquisadores avaliou a adequação de todos os dados, verificando eventuais erros. Quando havia alguma discrepância ou desvio incongruente, os dados eram verificados novamente por telefone. Quando isso não era possível, o paciente era convocado novamente para complementar os dados da entrevista. Os dados coletados foram digitados duas vezes para evitar erros na entrada desses e verificar a consistência interna.

3.3. Análise estatística

Artigo I

O curso dos transtornos psiquiátricos foi avaliado pelo indicador de persistência, calculado por meio da razão de prevalência (RP). Depois de calcular as estimativas de frequência para distúrbios atuais e transtornos ao longo da vida, definimos como razão de prevalência (RP): transtornos atuais/transtornos ao longo da vida.⁶⁸ A razão de prevalência foi multiplicada por cem e os valores para a persistência são expressos de zero a cem, onde quanto maior o valor, mais persistente é o padrão. Adequadamente, o intervalo de confiança de 95% (IC) para cada RP também foi determinado. Em seguida, avaliamos a coocorrência dos transtornos, por meio da análise de correlação tetracórica, para os grupos de transtorno bipolar, depressão, ansiedade, alimentação e transtornos por uso de substâncias. O número de comorbidades foi estimado para os transtornos atuais e transtornos ao longo da vida. Todas as análises foram realizadas com o Stata 13.0. O nível de significância foi 0,05 para testes bicaudais.

Artigo II

Para identificar ocorrência de possíveis classes de transtornos psiquiátricos entre os candidatos para cirurgia bariátrica, utilizou-se o método de análise de classe latente.⁷⁷ ACL é considerada a versão qualitativa da análise fatorial, que permite a identificação de variáveis latentes (não observáveis) de duas ou mais variáveis nominais/ordinais (observáveis).⁹² Análises preliminares das frequências e correlação entre as categorias diagnósticas do DSM-IV (Fig.1-Artigo II) determinaram a inclusão de variáveis categóricas (transtornos psiquiátricos). Para fins de análises dos dados, os transtornos bipolares I, II e outros não especificados (SOE) foram agrupados como "transtornos bipolares"; depressão maior, depressão menor e distímia como "transtornos depressivos"; pânico, agorafobia, fobia social, fobia específica, transtorno obsessivo-compulsivo, estresse pós-traumático e transtorno de ansiedade generalizada como "transtornos de ansiedade"; uso e dependência de álcool e drogas como "transtornos por uso de substâncias"; bulimia e compulsão alimentar como "transtornos alimentares". A análise inicial, por meio da correlação tetracórica, também revelou que os transtornos ao longo da vida apresentavam sintomas correlacionados significativamente na maioria dos pares²³, sugerindo a possibilidade de agrupamento em padrões regulares de comorbidade.

A modelagem da ACL indicou a representação por dois parâmetros: (1) a prevalência de cada classe e (2) a probabilidade condicional de solução na classe. O primeiro parâmetro descreveu a distribuição de classes latentes na amostra, indicando se a população era igualmente distribuída ao longo das classes ou se houve alguma que se destacava sobre outras. O segundo parâmetro representou as chances de um paciente de determinada classe apresentar os mesmos transtornos psiquiátricos, a fim de demonstrar que cada classe foi internamente homogênea. Esses parâmetros auxiliam na interpretação e identificação dos agrupamentos. O pressuposto da ACL quanto à independência local, verifica se a ocorrência de um distúrbio psiquiátrico particular não é associada à ocorrência de outro transtorno psiquiátrico dentro de uma determinada classe. Após checagem dos parâmetros, os transtornos ao longo da vida foram certificados de duas a cinco classes e avaliados por meio de resíduos condicionais bivariados.^{93,94} Valores de resíduos maiores que 1,96 indicaram uma violação em potencial da suposição de independência local.

Antes de determinar os parâmetros de interesse da ACL foi necessário definir o número de classes latentes existentes. Os modelos são ajustados com diferentes números de classes e comparados de acordo com estatísticas de ajuste de modelos e testes estatísticos. A decisão do número final das classes baseou-se nos critérios de informação de: Akaike (AIC), Bayesiano (BIC) e no critério Bayesiano ajustado (aBIC).^{95,96} Medidas de entropia, Vuong-Lo-Mendell-Rubin (VLMR), teste de razão de verossimilhança e a probabilidade de Lo-Mendell-Rubin (LMR), complementaram a avaliação do modelo. Wu (2009)⁹⁷ estudou modelos de ACL e comparou o desempenho dos quatro critérios em diferentes cenários. Concluiu que o BIC e o aBIC tiveram melhor desempenho na maioria dos cenários estudados. A magnitude da redução do valor de um determinado critério foi mensurada utilizando a variação percentual entre os critérios calculados para os modelos com k e $k-1$ classes, respectivamente.

Em relação à confiança com que os pacientes foram classificados nas classes latentes calculou-se a entropia relativa que é muito utilizada como uma estatística global da qualidade da classificação. Varia entre zero e um, e valores próximos de um indicam grau de confiança elevado na classificação definida pelo modelo, além de mostrar que existe uma adequada separação entre as classes latentes. Valores acima de 0,8 são considerados aceitáveis.⁹⁸

Testes estatísticos são uma forma menos subjetiva de se comparar modelos. O teste da Razão de Verossimilhanças (TRV), muito utilizado para a comparação de modelos encaixados, não pode ser utilizado na comparação de modelos de classes latentes com diferentes números de classes (apesar de serem considerados modelos encaixados) pois o teste aplicado nesse cenário não atende às condições de regularidade requeridas.⁹⁹ Como alternativa, baseando-se no trabalho de Vuong (1989), Lo, Mendell e Rubin (2001)^{95,96} propuseram uma aproximação para a distribuição do TRV que pode ser utilizada para comparar modelos de classes latentes encaixados. Dessa forma, em ambos os testes, na comparação de um modelo com k classes versus um modelo com $k-1$ classes, valores pequenos de p indicam que o modelo com k classes deve ser preferido ao modelo com $k-1$ classes. A ACL de múltiplos grupos na amostra total foi ajustada para examinar a possibilidade de um modelo assumir diferentes classes psicopatológicas nos subgrupos de homens e mulheres. O melhor modelo para mulheres e homens foi a solução de 3-classes. Esta decisão foi apoiada pela interpretação clínica das soluções e

valores elevados de entropia (0,80/0,91). O comando “*knownclass*” no software Mplus foi introduzido para ajustar os dados de 311 mulheres e 82 homens.

Tendo como referência a classe menos sintomática, denominada “oligossintomática”, realizou-se uma logística multinomial onde a regressão foi ajustada para verificar os efeitos das covariáveis. As seguintes variáveis demográficas: idade (anos), escolaridade (anos), estado civil (casado/união estável, separado/divorciado, solteiro, viúvo), IMC (kg/m²), e ocupação profissional (trabalhando, desempregado), foram gradualmente inseridas no modelo. Para as covariáveis “estado civil” e “ocupação”, as categorias “casado” e “trabalho” foram escolhidas, respectivamente, como categorias de referência. Educação, idade e IMC foram inseridas no modelo como variáveis contínuas. Toda vez que uma nova covariável era introduzida no modelo, o ajuste era determinado. As etapas foram: 1) Uma por vez, as covariáveis foram incluídas no modelo basal de classes latentes (modelo sem covariáveis) e as prevalências das classes latentes em cada modelo foram anotadas; 2) As covariáveis que não alteraram a prevalência do modelo basal em mais do que 1,5%, em módulo, foram selecionadas para serem incluídas no modelo final; 3) Ajustou-se todos os modelos correspondentes a todas as combinações possíveis das covariáveis selecionadas na etapa 2; 4) Novamente foram verificados e selecionados os modelos em que a prevalência do modelo basal não foi alterada em mais do que 1,5%, em cada módulo; 5) As estatísticas de ajuste dos modelos selecionados na etapa 4 foram analisadas com o intuito de selecionar o modelo final. As análises foram realizadas por meio do Mplus 6.12¹⁰⁰ versão de software 5 (www.statmodel.com) e R versão 3.2.1 (www.cran.org). O nível de significância assumida foi $p < 0,05$, para testes bicaudais.

3.4. Aspectos éticos

O presente estudo teve como referência amostral o estudo “Frequência de transtornos mentais em pacientes obesos candidatos à cirurgia bariátrica por meio de entrevista estruturada para transtornos do DSM-IV (SCID-I/P)”, aprovado pelo Comitê de Ética do Hospital das Clínicas da Faculdade de

Medicina de São Paulo-FMUSP, protocolo 0228/11 (Anexo I) e anuência de pesquisa interdepartamental do Departamento de Gastroenterologia FMUSP (Anexo II). Contou com o apoio da Fundação de Amparo à Pesquisa do Estado de São Paulo – FAPESP, processos 2012/17435-7 e 2012/17498-9.

4 – Resultados

4. 1 - Artigo 1

Morbidity persistence and comorbidity of mood, anxiety, and eating disorders among preoperative bariatric patients. Duarte-Guerra, L.S.; Coêlho, B.M.; Santo, M.A., Lotufo-Neto, F.; Wang, Y.P. Psychiatry Research. 257 (2017) 1-6. doi: 10.1016/j.psychres. 2017.07.020. Epub 2017 Jul 10.

Reprinted by permission by Psychiatry Research
from Elsevier and Copyright Clearance Center.
License Number: 4427591427843

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Morbidity persistence and comorbidity of mood, anxiety, and eating disorders among preoperative bariatric patients

Leorides Severo Duarte-Guerra^a, Bruno Mendonça Coêlho^a, Marco Aurélio Santo^b,
Francisco Lotufo-Neto^a, Yuan-Pang Wang^{a,*}

^a Department and Institute of Psychiatry (LIM-23), University of São Paulo Medical School, São Paulo, SP, Brazil

^b Department of Surgery, University of São Paulo Medical School, São Paulo, SP, Brazil

ARTICLE INFO

Keywords:

Psychiatric disorders
Psychopathology
Comorbidity
Obesity
Bariatric surgery

ABSTRACT

The current study investigates the patterns of disease persistence and comorbidity of psychiatric disorders among patients with class III obesity in pre-operative period. For 393 treatment-seeking patients with severe obesity recruited from a bariatric center, we ascertained their psychiatric diagnosis through Structured Clinical Interview for DSM-IV (SCID-I). Following, the frequency, persistence and comorbidity pattern of psychiatric disorders in this sample were determined. Current psychiatric disorders were observed in over half of patients during preoperative period, being anxiety disorders the most frequent diagnosis. For lifetime disorders, mood disorders were the most frequent diagnosis. Most of the sample presented 2 or more concurrent lifetime psychiatric disorders. While mood and eating disorders were frequent conditions, anxiety disorders were the most persistent conditions (the highest one month-to-lifetime prevalence ratio) and were significantly correlated with bipolar, depressive and eating disorders. Psychiatric disorders are frequent and enduring conditions among patients looking for bariatric surgery. Comorbid anxiety, mood, and eating disorders are remarkable features in treatment-seeking patients with obesity. Prognostic implications of preoperative psychiatric disorders on surgery outcome should be demonstrated prospectively in intervention studies.

1. Introduction

Obesity and mental disorders are burdensome health problems observed in general population and clinical samples. Existing surveys using operational diagnostic criteria of the DSM-IV system have reported that between 36.8% and 80.9% of patients with obesity before bariatric surgery presented at least any mental disorder throughout lifetime (Rosenberger et al., 2006; Mauri et al., 2008; Malik et al., 2014; Duarte-Guerra et al., 2015). Nevertheless, the impact of such high frequency of mental disorders in all stages of weight reduction process, in terms of percentage of excessive weight loss (%EWL), quality of life, adherence to follow-up and metabolic parameters is still poorly understood.

In accordance to a recent meta-analysis, binge eating disorder (BED) and depression are the most frequent single disorders in individuals seeking and undergoing weight reduction surgery, observed respectively in 17% and 19% of the samples (Dawes et al., 2016). Because active cases of psychiatric disorders can defer the indication of gastropasty surgery, proper identification and stabilization of pre-existing

clinical picture are essential requirements of pre-surgical evaluation. The trajectory of specific mental conditions, as well as the pattern of comorbidity phenotype in bariatric patients, might influence weight regain and worsening of quality of life during the follow-up period. Systematic evaluation of psychiatric disorders is recommended as key pre-surgical assessment in clinical practice guidelines published jointly by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery (Mechanick et al., 2013). Despite of knowledge on frequent association between mental disorders and severe obesity in bariatric samples, the pattern of course and comorbidity of psychiatric disorders are rarely investigated in patients with morbid obesity.

There is little consensus in definition of illness persistence and how its natural course can be operationalized (Schinnar et al., 1990). The uncertainty about the age of disease onset has prompted some scholars to focus on duration of treatment as indicator of disability and prognosis. Although the importance of continuous monitoring of the diagnosis of a patient is unquestionable, specific disease patterns, ethnic and cultural factors may intervene in the duration of a disease (Ruggeri

* Correspondence to: Departamento & Instituto de Psiquiatria (LIM-23), Faculdade de Medicina, Universidade de São Paulo, Rua Dr. Ovídio Pires de Campos, no. 785, CEP 05403-010 São Paulo, SP, Brazil.

E-mail address: gnap_inbox@hotmail.com (Y.-P. Wang).

<http://dx.doi.org/10.1016/j.psychres.2017.07.020>

Received 1 March 2017; Received in revised form 1 July 2017; Accepted 10 July 2017
Available online 10 July 2017

0165-1781/ © 2017 Elsevier B.V. All rights reserved.

et al., 2000). The persistence of a given disorder is often associated with the operative concept of severity, what can exert considerable impact on physical, emotional, intellectual, professional, social, and spiritual functioning of individuals. For instance, the persistence of preoperative psychopathology among bariatric candidates to gastroplastic surgery may influence %EWL outcome and quality of life in post-surgery period (Yen et al., 2014).

As such, traditional approach for documenting disease persistence has estimated lifetime morbidity risks by the means of survival analysis (Fuchs et al., 2010). Alternative approach also has analyzed disease persistence as the duration ratio between the proportion of current cases and lifetime cases, e.g., Kessler et al. (2012). Although epidemiological evidence has indicated that patients with chronic severe psychiatric disorders are more likely than the general population to be obese (Pickering et al., 2007), the pattern of disease persistence is still under-researched.

Poorer treatment compliance and unfavorable weight loss outcomes in population with obesity were more associated with co-occurrence of two or more psychiatric conditions than single disorder (Pataky et al., 2011). Psychiatric comorbidity has been shown as an aggravating factor of quality of life in both patients with obesity and normal weight ones (Carpiniello et al., 2009). Patterns of comorbidity might forecast post-surgical %EWL and quality of life during all phases of bariatric surgery (Pataky et al., 2011). Therefore, the effects of comorbidity (Schellevis, 1993) among those patients undergoing bariatric surgery may have a clinical implication as well as contributing explanation for worse outcome.

Few studies have analyzed the persistence and the patterns of comorbidity in patients with obesity in the preoperative period. Hidden forms of the disease are liable to unleash after surgical intervention (Kalarchian et al., 2008), for example, substance use disorders [SUD] (Svensson et al., 2013; Li and Wu, 2016). While pre-existing disorders diagnosed in pre-operative assessment can remain or even intensify after surgery, non-detected and new forms of psychopathology can occur during the follow-up period. This changeable instability of psychiatric disorders might affect the success of weight reduction procedures. In order to capture the morbidity course and co-occurrence of mental disorders among candidates to bariatric surgery, the aims of the current report were to investigate through structured psychiatric interview the persistence of psychiatric disorders and their pattern of comorbidity in the pre-operative period.

2. Methods

2.1. Subjects

Participants were recruited from the largest Brazilian bariatric surgery center and should meet the following inclusion criteria: a) class III obesity (BMI ≥ 40 kg/m²) or class II obesity plus medical comorbidity, b) aged 18 years or more, and c) able to understand the risks and benefits of gastroplastic surgery. After undertaking complete lab work-up and be approved by the multidisciplinary clinical staff, candidates were ranked in a waiting list in accordance to admission date and clinical severity.

The first 500 eligible subjects were consecutively invited by telephone to a personal interview, which is independent of pre-surgical evaluation process for undertaking bariatric surgery. Among them, 63 individuals declined to participate during telephone contact and 44 reported mobility difficulty, severe psychiatric illness, or previous bariatric surgery. The final sample of 393 patients yielded a participation rate of 78.6%.

The majority of participants were women (79.1%) and married (51.1%). Mean schooling level was 9.6 years (standard deviation (SD) 3.6), mean age 43.0 years (SD 11.5), and mean BMI 47.8 kg/m² (SD 7.5). Men presented higher preoperative BMI in comparison to women (50.2 vs. 46.4 kg/m², $p = 0.01$) (Table 1).

Table 1
Demographic characteristic of the sample.

Characteristic	(%)	N
Sex		
Female	79.1	311
Male	20.9	82
Marital status		
Single	25.4	100
Married	51.1	202
Widowed	6.6	26
Separated/divorced	16.5	65
Education		
8 years	35.1	138
11 years	44.5	175
15 years	18.1	71
Pos-graduation	2.3	9
mean Age, year (SD)	43.0 (11.5)	
mean BMI, kg/m ² (SD)	47.8 (7.5)	

SD: standard deviation.

BMI: body mass index.

2.2. Instrument

From 2010–2012, six trained clinicians applied the Structured Clinical Interview for DSM-IV Axis I (SCID-I) (First et al., 2002) to assess mental disorders. The SCID-I is a standardized semi-structured interview widely accepted as the gold standard to make diagnosis of psychiatric disorders listed in DSM-IV (American Psychiatric Association, 2000). After probing the presence of psychopathology, the interviewer should explore if the respondents meet the DSM-IV criteria for mood (section A, D), substance use disorders (SUD) (E), anxiety (F), and eating disorders (H). The diagnostic strategy adopted by SCID-I is top-down, i.e., the presence of symptoms should be checked for the criteria of the suspected psychiatric diagnosis. Considerable evidence of reliability and validity was reported in patient samples (Del-Ben et al., 1996).

For the present investigation, we used the patient version of SCID-I, which allowed recording disorders for both current and lifetime period. The current diagnosis assesses the presence of an active disorder during the past month, e.g., an episode of mood disorder. Otherwise, the interviewer must evaluate the retrospective evidence of past episode(s) of mental disorder. When patient reports multiple episodes, the most recent or the worst disease phase is considered as evidence of lifetime diagnosis. In present study, the inter-rater agreement for SCID-I lifetime disorders was determined as kappa coefficient of 0.81 in a random sample of 15 patients (Duarte-Guerra et al., 2015).

2.3. Statistical analysis

After computing the frequency estimates for current disorders and lifetime disorders, we defined as prevalence ratio (PR) to denote the one month-to-lifetime (1 M/LT) persistence of group of disorders (Kessler et al., 2012). This PR represents a proxy indicator of morbidity persistence and was ascertained by dividing the percentage of current disorders by lifetime disorders. Possible values range from 0 to 100, where the greater the figure, the more persistent pattern is. Accordingly, the 95% confidence interval (CI) for each PR also was determined.

The number of comorbid disorders was estimated for current and lifetime disorders. Following, we assessed the tetrachoric correlation for the groups of bipolar, depressive, anxiety, eating, and SUD. All analyses were performed with Stata 13.0. The level of significance was 0.05, for two-tailed tests.

Table 2

Frequency, persistence and number of comorbid psychiatric disorders among patients with severe obesity waiting for bariatric surgery ($N = 393$).

Psychiatric disorder	Current ^a N (%)	Lifetime ^a N (%)	1 M/LT	95% CI
Any psychiatric disorder	227 (57.8)	318 (80.9)	71.4	62.1–80.7
Mood disorder	85 (21.6)	255 (64.9)	33.3	26.2–40.4
Bipolar disorders	54 (13.7)	140 (35.6)	38.6	28.3–48.9
Bipolar disorder I	8 (2.0)	20 (5.1)	40.0	12.3–67.7
Bipolar disorder II	29 (7.4)	55 (14.0)	52.7	33.5–71.9
Bipolar not otherwise specified	17 (4.3)	65 (16.5)	26.2	13.7–38.6
Depressive disorders	31 (7.9)	115 (29.3)	27.0	17.5–36.4
Major depressive disorder	27 (6.9)	108 (27.5)	25.0	15.6–34.4
Dysthymia	4 (1.0)	5 (1.3)	80.0	1.6–158.4
Minor depressive disorder	–	2 (0.5)	–	NA
Anxiety disorders	182 (46.3)	215 (54.7)	84.7	72.4–96.9
Specific phobia	67 (17.0)	92 (23.4)	72.8	55.4–90.3
Social phobia	36 (9.2)	50 (12.7)	72.0	48.5–95.5
Agoraphobia	22 (5.6)	42 (10.7)	52.4	30.5–74.3
Anxiety not otherwise specified	21 (5.3)	21 (5.3)	100.0	57.2–142.8
Obsessive-compulsive disorder	14 (3.6)	25 (6.4)	56.0	26.7–85.3
Post-traumatic stress disorder	10 (2.5)	12 (3.1)	83.3	31.7–135.0
Panic disorder	9 (2.3)	35 (8.9)	25.7	8.9–42.5
Generalized anxiety disorder	94 (23.9)	–	–	NA
Substance use disorders	12 (3.1)	69 (17.6)	17.4	7.6–27.2
Alcohol use disorder	12 (3.1)	57 (14.5)	21.1	9.1–33.0
Drug use disorder	2 (0.5)	27 (6.9)	7.4	2.9–17.7
Eating disorders	79 (20.1)	138 (35.1)	57.2	44.6–69.9
Binge eating disorder	65 (16.5)	117 (29.8)	55.6	42.0–69.1
Bulimia nervosa	14 (3.6)	36 (9.2)	38.9	18.5–59.3
Comorbidity pattern				
No disorder	166 (42.2)	75 (19.1)		
1 disorder	105 (26.7)	75 (19.1)		
2 disorders	61 (15.5)	89 (22.6)		
3 disorders +	61 (15.5)	154 (39.2)		

1M/LT: One month-to-lifetime prevalence ratio (PR) to denote persistence, range 0–100.

^a The frequency rates of current and lifetime diagnosis of psychiatric disorders are based on the Structured Clinical Interview for DSM-IV Axis I (SCID-I).

2.4. Ethics of the study

The Ethics Committee of the University of São Paulo approved the study. All participants have signed an informed consent and were secured that no information provided would influence their eligibility for surgery or list ranking.

3. Results

Table 2 depicts the frequency of current and lifetime psychiatric disorders, the prevalence ratio (PR) for denoting persistence, and the number of comorbid conditions. Over half (57.8%) of surgery-seeking obese subjects met the criteria for any current psychiatric disorders.

Table 3

Tetrachoric correlation between pairs of lifetime psychiatric disorders among patients with severe obesity ($N = 393$).

	Bipolar Disorders	Depressive Disorders	Anxiety Disorders	Substance Use Disorders	Eating Disorders
Bipolar Disorders	1.00				
Depressive Disorders ^a	–1.00***	1.00			
Anxiety Disorders	0.36***	0.23**	1.00		
Substance Use Disorders	0.66***	0.35**	0.17	1.00	
Eating Disorders	0.35***	0.01	0.35***	0.20 [†]	1.00

*** $p < 0.0001$.

** $p < 0.005$.

* $p < 0.05$.

^a include major depressive disorders and dysthymia.

Anxiety disorders were the most frequent diagnosis (46.3%). Mood, eating disorders and SUD were respectively diagnosed in 21.6%, 20.1% and 3.1% of the sample.

The lifetime rate of any psychiatric disorders was 80.9%. Mood disorders were the most frequent class (64.9%), where around one-third of the sample met the diagnosis of bipolar and depressive disorders. The second most frequent class (54.7%) was anxiety disorders. Eating disorders were diagnosed in 35.1% of the sample and a lifetime history of binge eating disorders (BED) was reported by 29.8% of participants.

Regarding the course of disorders, high persistence was a prominent feature (PR = 71.4) in this bariatric sample. Comparing all groups, anxiety disorders were the most persistent class (PR = 84.7), being posttraumatic stress disorder (PTSD) the most long-lasting single disorder in the class (PR = 83.3).

Subsequently, moderate persistence was observed among eating disorders (PR = 57.2), being BED the most persistent disorder (PR = 55.6). Mood disorders (depression and mania/hypomania episode) and SUD appeared to be unstable during lifetime, respectively PR 33.3 and 17.4.

Concerning comorbidity, 31% of patients with severe obesity presented two or more comorbid disorders at the time of assessment. Over half of patients (61.8%) presented two or more lifetime disorders. Variable patterns of comorbidity were observed for pairs of disorder (Table 3). Bipolar disorders (BD) were significantly correlated with all disorder classes ($p < 0.0001$). Depressive disorders were correlated with anxiety and SUD, but not with eating disorders ($p > 0.05$). Anxiety disorders did not correlate with SUD. Noteworthy, eating disorders were most correlated with BDs and anxiety disorders ($p < 0.0001$).

4. Discussion

Severe obesity is a multifactorial condition, characterized by excess bodyweight and unfavorable health consequences. In present study, the association between obesity and psychiatric disorders was investigated through standard SCID-I interview, in terms of disease persistence and comorbidity clustering. Anxiety disorders in this sample of 393 surgery-seeking patients stood out, because this group of disorders occurred at higher frequency and more persistent course. More rule than exception, disorder comorbidity was the major clinical presentation in almost two-third of candidates to bariatric surgery. In special, bipolar disorders (BD) presented significant correlation with all other psychiatric conditions. The current investigation may contribute to better systematization of pre-operative assessments, as well further understanding of hypothetical causal relationship. Pre-surgical psychopathological configurations of psychiatric disorders might present potential impact for treatment and follow-up of post-operative outcome, in terms of %EWL, metabolic parameters, and compliance to clinical management (Kinzl et al., 2006; Gorin and Raftopoulos, 2009; Rutledge et al., 2009).

4.1. Morbidity persistence

Typically, anxiety presents an enduring course and is regularly

associated with other psychiatric conditions among individuals with obesity (Garipey et al., 2010). However, its obesogenic effect has been less investigated in comparison with other comorbidities associated with obesity, e.g., mood and eating disorders. Effect of comorbid anxiety in perpetuating and worsening obesity during lifespan was relatively overlooked in the literature on bariatric surgery (De Zwaan et al., 2011; Wedin et al., 2012). Hence, mitigating persistent anxiety symptoms emerges as a relevant clinical target to be considered during both pre- and post-operative period.

For instance, PTSD was the most persistent single anxiety condition in the current study, since conditioned fear responses can last for decades after the exposure to traumatic event (VanElzakker et al., 2014). Also, the joint relationship between life adversity, PTSD and obesity must be established in view of their persistence and pattern of comorbidity with other psychiatric disorders (e.g., mood, SUD and eating disorders) among bariatric samples (Pagoto et al., 2012).

Whilst mood disorders are the most frequent lifetime disorders among obese individuals (Simon et al., 2006), their episodic course that wanes and waxes must be addressed before undertaking surgery and be monitored during the post-surgery follow-up. Frequently, mood symptoms decrease after bariatric surgery, due to patient's satisfaction with self-image and improvement of quality of life associated with %EWL (De Zwaan, 2012). Depressive symptoms have been investigated among patients seeking the bariatric procedure through assessment scales (Duarte-Guerra et al., 2016; Schutt et al., 2016). Further emergence of post-operative manic/hypomanic symptoms are described in several studies (Kalarchian et al., 2008; Ahmed et al., 2013; Godini et al., 2016), as well as their frequent co-occurrence with additional psychiatric conditions (Da Silva et al., 2015). Because the exact effect of gastroplastic surgery on stability of mood disorders is not fully understood (Munoz et al., 2007), some bariatric centers have included non-stabilized depressive and manic phases as contraindication to undertake surgery (Bauchowitz et al., 2005). Although mood disorders are the most frequent lifetime disorders in the bariatric setting, their episodic course requires careful assessment during all treatment phases.

Hypothetical dysfunction in hypothalamic-pituitary-adrenal axis, neurotransmitter systems, and brain-derived neurotrophic factor in both BDs and obesity was suggested as common neurobiological abnormalities that may suggest bidirectional causal relationship between those conditions (McElroy and Keck, 2014). For instance, successful use of lithium among bariatric patients has been reported in the literature (Bingham et al., 2016).

Eating disorders has been more extensively investigated than mood and anxiety disorders in samples of individuals with obesity (Burgmer et al., 2005; Gammelmark et al., 2015). Our data on this bariatric sample are in line with the literature reporting a pattern of moderate persistence (Zaider et al., 2002). In terms of post-operative assessment, it is true that episodes of binge eating decline after bariatric surgery, because adherence to nutritional program and inability to consume unusually large amounts of food as defined by BED diagnosis criteria (Bulik et al., 2007). In addition, new forms of abnormal eating behavior disorders develop and require further follow-up in post-surgery period, e.g., loss of control overeating and snacking small amounts of food can appear or re-appear after surgery (Conceição et al., 2015; Mitchell et al., 2015). Given important changes introduced after surgery, with direct interference in the gastrointestinal system, the eating disorders should be investigated as a separate group. Previous belief that pre-existing BED can predict post-surgical weight gain was demonstrated to be unproven in prospective studies (Wadden et al., 2006; Shakory et al., 2015). Therefore, preoperative BED provides, by itself, no motives for physicians to defer patients with severe obesity from bariatric surgery.

The self-medication hypothesis of using psychoactive medications and substances to reduce distressing psychiatric symptoms or weight control purpose is still under-researched (Khantzian, 1997). For example, recent literature reports the increase of new-onset cases of SUD among bariatric patients after the surgery (Svensson et al., 2013; Li and

Wu, 2016). In this perspective, meticulous assessment of psychiatric disorders in both preoperative and post-surgical period is required to estimate the impact of each type of disorder and the profile of comorbidity on weight control and quality of life (Mechanick et al., 2013).

4.2. Comorbidity of psychiatric disorders

Recent debates on comorbidity have pointed to artefactual effect of current system of classification (Maj, 2005), but the very nature of psychopathology remained elusive. Even in well-designed large samples, such as the Multi Generation Register in Sweden (Welch et al., 2016) and the Stanley Foundation Bipolar Treatment Outcome Network (McElroy et al., 2011), the relationship between obesity and different psychiatric disorders cannot be firmly established. Systematic surveys addressing the occurrence of psychiatric comorbidity among samples of patients with morbid obesity are scant (Fuchs et al., 2016). Reducing different psychopathologies into relevant dimensions might contribute to current debate on clinical utility of psychiatric classification and causal reasoning of mental disorders (Kotov et al., 2017).

In our sample of bariatric patients, almost two-third of treatment-seeking individuals presented two or more psychiatric disorders. This pattern of correlation between different disorders outnumbers the probability by chance of comorbidity to emerge, when compared with general population (Kessler et al., 2005). Therefore, potential relationship between class III obesity and psychiatric comorbidity can be suggested, with additive consequence in terms of severity, disability, quality of life, burden, and use of service.

BDs are the group with more comorbid disorders by far (McElroy and Keck, 2014), what worsen the general mental health of patients with comorbid obesity and BD. Spectrum approach of BD indicates that many clinical pictures remain in quiescent form or subclinical presentation, being masked by other comorbidities (Alciati et al., 2007). Active investigation of BD in patients with high level of comorbidity ought to be conducted in all stages of surgical procedure. Euphoria and manic symptoms are reported in post-operative period in bariatric patients (Nepal et al., 2015). However, this occurrence seems to be uncommon course in a prospective study after gastroplastic procedure (Kalarchian et al., 2016). Full-bloom manic episode occurring after surgical intervention could either be a natural recurrence of a manic episode or due to previously unknown mechanism during the post-surgical period. The controversial role of precipitation of new-onset BD due to surgery and its role with %EWL needs be better investigated in larger samples of BD patients with obesity (Grothe et al., 2014). Careful assessment of subtle symptoms of previous mania in a patient who has undergone recent bariatric surgery needs be considered as clinical routine to propose early therapeutics and prevent patient suffering (Marek et al., 2016).

Anxiety disorders are the most common and chronic mental disorders in the group of patients with obesity. Possibly, their chronic course facilitates comorbidities to emerge. Due to their low severity with less disabling impact in daily life, this group has being relatively overlooked by surgeons. Noteworthy is the lack of relationship between anxiety disorders with SUD, what can be hypothesized as the effect of anxiety relief by substances among patients with obesity. Because the anxiety often remains unchanged for long-lasting periods, this group of disorders must be investigated as bidirectional co-occurrence of obesity (Garipey et al., 2010). Targeting anxiety disorders in the population of patients with obesity may improve therapeutic success in the course of bariatric procedures.

Binge eating disorders (BED) appear to be associated with obesity, where symptoms used to co-occur and overlap (van der Hofstadt Román et al., 2016). In comparison with other groups of psychiatric disorders, the frequency of BED varies in accordance with healthcare service and treatment seeking samples (Mauri et al., 2008). In line with a large multi-site study (Woldeyohannes et al., 2016), our study showed that

there is a salient correlation between BED and BDs, but weaker relationship was observed with depressive disorders. DSM-5-based eating disorders are prevalent among BD patients, being associated with substantial psychiatric and medical illness burden (McElroy et al., 2016). Further investigations addressing this comorbidity constitute a meaningful avenue for better understanding and therapeutics of the population with obesity.

Finally, obesity should be regarded as a disease of complex etiology, which comorbid patterns of illnesses suggest that patients with hitherto mental illness and/or disordered eating are vulnerable to poorer outcome following bariatric surgery (Jarolimova et al., 2013). We highlight the need of systematic assessment, at the light of reliable methods, to track the course, pattern of comorbidity, natural history and weight loss response in all stages of treatment.

4.3. Limitations

Some limitations should be considered in current article. First, selection bias might have affected the representativeness of the sample of surgery-seeking patients with obesity recruited from a single hospital. However, the sample size is appropriate and excessive frequency of psychiatric disorders in our study is similar to reported rates in literature and higher than general population (Dawes et al., 2016).

Second, the use of SCID allowed identifying only active cases of mental disorders in the month prior to interview for current diagnosis. For example, cyclic disorders like recurrent depressive disorders and bipolar disorders might have been interviewed during their remitted phase of natural course or under adequate control of mood symptoms. We don't have information on stable remission of these cyclic disorders in the last three years for this cross-sectional study. Therefore, any scrutiny on these disorders of variable course must be understood taking into account the assessment method we adopted.

Third, to the extent that prevalence of SUD was lower than expected, our estimate might have been affected by the social desirability bias of impression management and use of face-to-face interview. We were not able to estimate the magnitude of SUD under-reporting in this sample. However, the figures for SUD found in present study were similar and in line with studies with comparable methodology (Mühlhans et al., 2009; Dawes et al., 2016). Furthermore, we have not prospectively determined new-onset cases of SUD, commonly reported in the literature.

Finally, though strong between-disorder correlation have suggested a persistent course of comorbidity relationship, replication sample is warranted in the future to determine which specific psychosocial and behavioral factors influence health outcomes during post-surgery period. Although the age of onset of psychiatric disorders was not recorded in current study, probably all disorders have already fully manifested in our sample at the mean age of 43.0 year.

Post-operative follow-up of the impact of psychiatric disorders comorbidity must be conducted to document its prognostic value, in terms of treatment adherence, quality of life and weight control. Moreover, latent form and subclinical disorders must be carefully identified before and after surgical intervention.

5. Comments

Mental disorders are indubitably associated with severe obesity. However, there is a variable persistence in the clinical picture, as well as the pattern of comorbidity clustering of surgery-seeking patients with obesity. More than systematic assessment and stabilization of the disorders in the pre-surgical period, regular and thorough evaluation of the candidates to obesity surgery during all stages of their weight loss process is mandatory.

Some persistent psychiatric disorders may identify a group of patients who are at risk for sub-optimal %EWL, poor treatment adherence, weight regains, and adverse outcomes. The effect of different patterns

of preoperative psychopathology in bariatric samples remains to be determined. Because the influence of intra-individual comorbidity of mental disorders on post-surgical weight outcome is still poorly investigated, rigorous prospective investigations are required to evaluate the relationship between the trajectory of pre-surgery psychiatric conditions and post-operative health outcomes.

Funding information

This investigation received grant from the Foundation for Research Support of the State of São Paulo (FAPESP # 2012/17435-7); Y-P.W. is the recipient of this grant. L. S. D. G. received a scholarship from the Foundation for Research Support of the State of São Paulo (FAPESP # 2012/17498-9).

Disclosure

The authors declare no conflict of interest

Acknowledgment

None.

References

- Ahmed, A.T., Warton, E.M., Schaefer, C.A., Shen, L., McIntyre, R.S., 2013. The effect of bariatric surgery on psychiatric course among patients with bipolar disorder. *Bipolar Disord.* 15 (7), 753–763.
- Alciati, A., D'Ambrosio, A., Foschi, D., Corsi, F., Mellado, C., Angst, J., 2007. Bipolar spectrum disorders in severely obese patients seeking surgical treatment. *J. Affect Disord.* 101 (1–3), 131–138.
- American Psychiatric Association, 2000. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. Author, Washington DC.
- Bauchowitz, A.U., Gonder-Frederick, L.A., Olbrisch, M.E., Azarbad, L., Ryee, M.Y., Schirmer, B., et al., 2005. Psychosocial evaluation of bariatric surgery candidates: a survey of present practices. *Psychosom. Med.* 67 (5), 825–832.
- Bingham, K.S., Thoma, J., Hawa, R., Sockalingam, S., 2016. Perioperative lithium use in bariatric surgery: a case series and literature review. *Psychosomatics* 57 (6), 638–644.
- Bulik, C.M., Brownley, K.A., Shapiro, J.R., 2007. Diagnosis and management, of binge eating disorder. *World Psychiatry* 6 (3), 142–148.
- Burgmer, R., Grigutsch, K., Zipfel, S., Wolf, A.M., de Zwaan, M., W., Herpertz, S., et al., 2005. The influence of eating behavior and eating pathology on weight loss after gastric restriction operation. *Obes. Surg.* 15 (5), 684–691.
- Carpiniello, B., Pina, F., Pillai, G., Nonnoi, V., Pisano, E., Corrias, S., et al., 2009. Psychiatric comorbidity and quality of life in obese patients. Results from a case-control study. *Int. J. Psychiatry Med.* 30 (1), 63–78.
- Conceição, E.M., Utzinger, L.M., Pisetsky, E.M., 2015. Eating disorders and problematic eating behaviours before and after bariatric surgery: characterization, assessment and association with treatment outcomes. *Eur. Eat. Disord. Rev.* 23 (6), 417–425.
- Da Silva, V.B., Da Silva, R.B., Azorin, J.M., Belzeaux, R., 2015. Mood disorders are highly prevalent but underdiagnosed among patients seeking bariatric surgery. *Obes. Surg.* 25 (3), 543–544.
- Dawes, A.J., Maggard-Gibbons, M., Maher, A.R., Booth, M.J., Miake-Lye, I., Shekelle, P.G., et al., 2016. Mental health conditions among patients seeking and undergoing bariatric surgery. *JAMA* 315 (2), 150–163.
- Del-Ben, C.M., Rodrigues, C.R., Zuardi, A.W., 1996. Reliability of the portuguese version of the structured clinical interview for DSM-III-R (SCID-I) in a brazilian sample of psychiatric outpatients. *Braz. J. Med Biol. Res.* 29, 1675–1682.
- De Zwaan, M., Enderle, J., Wagner, S., Mühlhans, B., Ditzén, B., Gefeller, O., et al., 2011. Anxiety and depression in bariatric surgery patients: a prospective, follow-up study using structured clinical interviews. *J. Affect Disord.* 133 (1–2), 61–68.
- De Zwaan, M., 2012. Could surgery influence psychopathology more in the long-term than evidence-based psychotherapy? Pros and cons of bariatric surgery in the treatment of obesity. *Verhaltenstherapie* 22, 199–203.
- Duarte-Guerra, L.S., Coêlho, B.M., Santo, M.A., Wang, Y.P., 2015. Psychiatric disorders among obese patients seeking bariatric surgery: results of structured clinical interviews. *Obes. Surg.* 25 (5), 830–837.
- Duarte-Guerra, L.S., Gorenstein, C., Paiva-Medeiros, P.F., Santo, M.A., Lotufo Neto, F., Wang, Y.P., 2016. Clinical utility of the Montgomery-Asberg Depression Rating Scale for the detection of depression among bariatric surgery candidates. *BMC Psychiatry* 16, 119.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 2002. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I/P)*. Biometrics Research: New York State Psychiatric Institute, New York (Research version, patient edition).
- Fuchs, C., Steinberg, D.M., Poyurovsky, M., 2010. On the estimation and comparison of lifetime morbid risks. *J. Data Sci.* 8, 645–664.
- Fuchs, H.F., Laughter, V., Harnsberger, C.R., Broderick, R.C., Berducci, M., DuCoin, C.,

- et al., 2016. Patients with psychiatric comorbidity can safely undergo bariatric surgery with equivalent success. *Surg. Endosc.* 30 (1), 251–258.
- Gammelmark, C., Jensen, S.O., Plessen, K.J., Skadhede, S., Larsen, J.T., Munk-Jørgensen, P., 2015. Incidence of eating disorders in danish psychiatric secondary healthcare 1970–2008. *Aust. N.Z. J. Psychiatry* 49 (8), 724.
- Garipey, G., Nitka, D., Schmitz, N., 2010. The association between obesity and anxiety disorders in the population: a systematic review and meta-analysis. *Int. J. Obes.* 34 (3), 407–419.
- Godini, L., Castellini, G., Facchiano, E., Lucchese, M., Ricca, V., 2016. Mood disorders and bariatric surgery patients: pre- and post- surgery. Clinical course – an overview. *J. Obes. Weight-Loss Med.* 2, 012.
- Gorin, A.A., Raftopoulos, I., 2009. Effect of mood and eating disorders on the shortterm outcome of laparoscopic Roux-en-Y gastric bypass. *Obes. Surg.* 19 (12), 1685–1690.
- Grothe, K.B., Mundi, M.S., Himes, S.M., Sarr, M.G., Clark, M.M., Geske, J.R., et al., 2014. Bipolar disorder symptoms in patients seeking bariatric surgery. *Obes. Surg.* 24 (11), 1909–1914.
- Jarolimova, J., Tagoni, J., Stern, T.A., 2013. Obesity: its epidemiology, comorbidities, and management. *Prim. Care Companion CNS Disord.* 15, 5.
- Kalarchian, M.A., Marcus, M.D., Levine, M.D., Soulakova, J.N., Courcoulas, A.P., Wisinski, M.S.C., 2008. Relationship of psychiatric disorders to 6-month outcomes after gastric bypass. *Surg. Obes. Relat. Dis.* 4 (4), 544–549.
- Kalarchian, M.A., King, W.C., Devlin, M.J., Marcus, M.D., Garcia, L., Chen, J.Y., et al., 2016. Psychiatric disorders and weight change in a prospective study of bariatric surgery patients: a 3-years follow-up. *Psychosom. Med.* 78 (3), 373–381.
- Kessler, R.C., Chiu, W.T., Demler, O., Merikangas, K.R., Walters, E.E., 2005. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the national comorbidity survey replication. *Arch. Gen. Psychiatry* 62 (6), 617–627.
- Kessler, R.C., Avenevoli, S., Costello, E.J., Georgiades, K., Green, J.G., Gruber, M.J., et al., 2012. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the national comorbidity survey replication adolescent supplement. *Arch. Gen. Psychiatry* 69 (4), 372–380.
- Khantzian, E.J., 1997. The self-medication hypothesis of substance use disorders: a re-consideration and recent applications. *Harv. Rev. Psychiatry* 4 (5), 231–244.
- Kinzel, J.F., Schrattecker, M., Traweger, C., Mattesich, M., Fiala, M., Biehl, W., 2006. Psychosocial predictors of weight loss after bariatric surgery. *Obes. Surg.* 16, 1609–1614.
- Kotov, R., Krueger, R.F., Watson, D., Achenbach, T.M., Althoff, R.R., Bagby, R.M., et al., 2017. The hierarchical taxonomy of psychopathology (HiTOP): a dimensional alternative to traditional nosologies. *J. Abnorm. Psychol.* 126 (4), 454–477.
- Li, L., Wu, L.T., 2016. Substance use after bariatric surgery: a review. *J. Psychiatr. Res.* 76, 16–29.
- Maj, M., 2005. Psychiatric comorbidity: an artefact of current diagnostic systems? *Br. J. Psychiatry* 186 (3), 182–184.
- Malik, S., Mitchell, J.E., Engel, S., Crosby, R., Wonderlinch, S., 2014. Psychopathology in bariatric surgery candidates: a review of studies using structured diagnostic interviews. *Compr. Psychiatry* 55 (2), 248–259.
- Marek, R.J., Ben-Porath, Y.S., Heinberg, L.J., 2016. Understanding the role of psychopathology in bariatric surgery. *Obes. Rev.* 17 (2), 126–141.
- Mauri, M., Rucci, P., Calderone, A., Santini, F., Oppo, A., Rinaldi, S., et al., 2008. Axis I and II disorders and quality of life in bariatric surgery candidates. *J. Clin. Psychiatry* 69, 295–301.
- McElroy, S.L., Frye, M.A., Helleman, G., Altschuler, L., Leverich, G.S., Suppes, T., et al., 2011. Prevalence and correlates of eating disorders in 875 patients with bipolar disorders. *J. Affect. Disord.* 128 (3), 191–198.
- McElroy, S.L., Keck Jr., P.E., 2014. Metabolic syndrome in bipolar disorder: a review with a focus on bipolar depression. *J. Clin. Psychiatry* 75 (1), 46–61.
- McElroy, S.L., Crow, S., Blom, T.J., Biernacka, J.M., Winham, S.J., Geske, J., et al., 2016. Prevalence and correlates of DSM-5 eating disorders in patients with bipolar disorder. *J. Affect. Disord.* 191, 216–221.
- Mechanick, J.I., Youdim, A., Jones, D.B., Garvey, W.T., Hurley, D.L., McMahon, M.M., et al., 2013. American Association of clinical endocrinologists; obesity society; American Society for metabolic & bariatric surgery. clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient – 2013 update: cosponsored by American Association of Clinical Endocrinologists. *Obes. Soc. Am. Soc. Metab. Bariatr. Surg. Obes.* 21 (Suppl.1), S1–S27.
- Mitchell, J.E., King, W.C., Courcoulas, A., Dakin, G., Elder, K., Engel, S., et al., 2015. Eating behavior and eating disorders in adults before bariatric surgery. *Int. J. Eat. Disord.* 48 (2), 215–222.
- Mühlhans, B., Horbach, T., de Zwaan, M., 2009. Psychiatric disorders in bariatric surgery candidates: a review of the literature and results of a German prebariatric surgery sample. *Gen. Hosp. Psychiatry* 31 (5), 414–421.
- Munoz, D.J., Chen, E., Fischer, S., Roehring, M., Sanchez-Johnson, L., Alverdy, J., et al., 2007. Considerations for the use of the Beck Depression Inventory in the assessment of weight-loss surgery seeking patients. *Obes. Surg.* 17 (8), 1097–1101.
- Nepal, H., Bhattarai, M., Agustin, E.T., 2015. New-onset mania following bariatric surgery. *Psychiatry Investig.* 12 (1), 152–154.
- Pagoto, S.L., Scheider, K.L., Bodenlos, J.S., Appelhans, B.M., Whited, M.C., Ma, Y., et al., 2012. Association of post-traumatic stress disorder and obesity in a nationally representative sample. *Obesity* 20 (1), 200–205.
- Pataky, Z., Carrad, I., Golay, A., 2011. Psychological factors and weight loss in bariatric surgery. *Curr. Opin. Gastroenterol.* 27 (2), 167–173.
- Pickering, R.P., Grant, B.F., Chou, S.P., Compton, W.M., 2007. Are overweight, obesity, and extreme obesity associated with psychopathology? Results from the national epidemiologic survey on alcohol and related conditions. *J. Clin. Psychiatry* 68, 998–1009.
- Rosenberger, P.H., Henderson, K.E., Grilo, C.M., 2006. Psychiatric disorder comorbidity and association with eating disorders in bariatric surgery patients: a cross-sectional study using structured interview-based diagnosis. *J. Clin. Psychiatry* 67, 1080–1085.
- Ruggeri, M., Leese, M., Thornicroft, G., Bisoffi, G., Tansella, M., 2000. Definition and prevalence of severe and persistent mental illness. *Br. J. Psychiatry* 177 (2), 149–155.
- Rutledge, T., Groesz, L.M., Savu, M., 2009. Psychiatric factors and weight loss patterns following gastric bypass surgery in a veteran population. *Obes. Surg.* 21 (1), 29–35.
- Schellevis, F.G., 1993. Chronic Disease in General Practice. Comorbidity and Quality of Care. Drukkerij Pascal, Utrecht.
- Schinnar, A.P., Rothbard, A.B., Kanter, R., Jung, Y.S., 1990. An empirical literature review of definition of severe and persistent mental illness. *Am. J. Psychiatry* 147 (12), 1602–1608.
- Schutt, P.E., Kung, S., Clark, M.M., Koball, A.M., Grothe, K.B., 2016. Comparing the Beck Depression Inventory-II (BDI-II) and Patient Health Questionnaire (PHQ-9) depression measures in an outpatient bariatric clinic. *Obes. Surg.* 26 (6), 1274–1278.
- Shakory, S., Van Exan, J., Mills, J.S., Keating, L., Sockalingam, S., Taube-Schiff, M., 2015. Binge eating in bariatric surgery candidates: the role of insecure attachment and emotion regulation. *Appetite* 91, 69–75.
- Simon, G.E., Von Korff, M., Saunders, K., Miglioretti, D.L., Crane, P.K., van Belle, G., et al., 2006. Association between obesity and psychiatric disorders in the US adult population. *Arch. Gen. Psychiatry* 63 (7), 824–830.
- Svensson, P.A., Anveden, Å., Romeo, S., Peltonen, M., Ahlin, S., Burza, M.A., et al., 2013. Alcohol consumption and alcohol problems after bariatric surgery in the Swedish obese subjects study. *Obesity* 21 (12), 2444–2451.
- Van der Hofstadt Román, C.J., Costa, C.L., Gonzalez, S.T., Rodriguez, M.G., Martinez, E.P., Rodriguez-Marin, J., 2016. Predictors of anxiety and depression symptoms in bariatric surgery candidates. *Bariatr. Surg. Pract. Care* 11 (3), 123–130.
- VanElzakker, M.B., Dahlgren, M.K., Davis, F.C., Dubois, S., Shin, L., 2014. From Pavlov to PTSD: the extinction of conditioned fear in rodents, humans, and in anxiety disorders. *Neurobiol. Learn. Mem.* 113, 3–18.
- Wadden, T.A., Sarwer, D.B., Williams, N.N., 2006. Behavioral assessment and characteristics of patients seeking bariatric surgery. *Obesity* 14 (Suppl 2), S1S–S2S.
- Wedin, S., Byrne, K., Morgan, K., Lepage, M., Goldman, R., Crowley, N., et al., 2012. Presurgical weight is associated with pain, functional impairment, and anxiety among Gastric Bypass surgery patients. *Pain Res. Treat.* 2012, 412174.
- Welch, E., Jangmo, A., Thornton, L.M., Norring, C., von Hausswolt-Juhlin, Y., Herman, B.K., et al., 2016. Treatment-seeking patients with binge-eating disorder in the swedish national registers: clinical course and psychiatric comorbidity. *BMC Psychiatry* 16, 163.
- Woldeyohannes, H.O., Soczynska, J.K., Maruschak, N.A., Syeda, K., Wium-Andersen, I.K., Lee, Y., et al., 2016. Binge eating in adults with disorders: results from the international mood disorders collaborative project. *Obes. Res. Clin. Pract.* 10 (5), 531–543.
- Yen, Y.C., Huang, C.K., Taic, C.M., 2014. Psychiatric aspects of bariatric surgery. *Curr. Opin. Psychiatry* 27 (5), 374–379.
- Zaider, T.I., Johnson, J.G., Cockell, S.J., 2002. Psychiatric disorders associated with the onset and persistence of bulimia nervosa and binge eating disorder during adolescence. *J. Youth Adolesc.* 31 (5), 319–329.

4.1.1 – Discussão do artigo I

O artigo “*Morbidity, persistence and comorbidity of mood, anxiety, and eating disorders among preoperative bariatric patients*”, apresentou o curso e a coocorrência das morbidades dos transtornos mentais entre os candidatos à cirurgia bariátrica. As análises primárias das frequências dos transtornos no momento da entrevista, e dos transtornos ao longo da vida, mostraram que os transtornos do humor, apesar de muito frequentes em vida, no momento da entrevista declinaram. Os transtornos do humor são mais reconhecidos e passíveis de tratamento, o que justifica o declínio de sua frequência ao longo da vida.¹⁰¹ Entretanto, o mesmo não ocorreu com os transtornos de ansiedade, que mantiveram as mesmas frequências tanto ao longo da vida como no momento atual. Desse modo, o objetivo foi investigar a persistência dos transtornos e a coocorrência dos transtornos por meio da razão de prevalência-atual com prevalência-vida e da correlação tetracórica, respectivamente. A fórmula da razão da prevalência, apesar de não tão comum na literatura, mostra-se um recurso estatístico eficiente para avaliar proporcionalidade. O cálculo da correlação tetracórica, por sua vez, é mais recomendado na literatura como eficiente ferramenta para analisar correlações.

Os transtornos de ansiedade, além de frequentes, foram os mais persistentes. Minha prática clínica mostra que o próprio paciente, assim como a equipe multidisciplinar, subestimam manifestações ansiogênicas; compreendem os sintomas de ansiedade como comportamentos característicos de indivíduos com obesidade e não como patologia. Assim, a persistência da doença pode ser decorrente da falta de tratamento e monitoramento dos sintomas como uma psicopatologia. Diferentemente dos transtornos de humor, que são os mais frequentes e são associados como agravantes ou desencadeantes da obesidade e recebem tratamentos e acompanhamentos adequados.⁴⁸ Os transtornos de ansiedade seguem um curso único: quando acompanhados em seguimento, observa-se que eles não declinam após o procedimento cirúrgico.¹⁰² O curso persistente está associado a outras condições psiquiátricas, que podem levar à incapacitação, e ao insucesso no prognóstico cirúrgico.¹⁰³

Em segundo plano, investigamos a concomitância dos transtornos psiquiátricos em pacientes com obesidade candidatos à cirurgia. Esta análise partiu da observação

que dois terços da amostra apresentaram três ou mais transtornos mentais. Pesquisas sistemáticas que abordam a ocorrência de comorbidade psiquiátrica entre amostras de pacientes com obesidade mórbida são escassas.⁶⁷ A relação entre obesidade grau III e comorbidades tem consequências que se somam em termos de gravidade, incapacitação, qualidade de vida pior e sobrecarga no uso do serviço médicos. Neste primeiro artigo, nosso achado foi que, dentre os transtornos psiquiátricos em pacientes pré-cirúrgicos, o transtorno bipolar, apesar de não ser tão frequente, compõe grupo mais comórbido.¹⁰⁴ A forma grave e incapacitante do transtorno bipolar ainda não foi devidamente explorada no cenário da cirurgia bariátrica. Os transtornos bipolares, assim como o transtornos de ansiedade, são subvalorizados juntos a profissionais ligados aos procedimentos da cirurgia bariátrica. O que existe hoje na literatura ainda não é consensual; há estudos que mostram que a forma espectral dos transtornos bipolares, existentes na fase pré-cirúrgica, eclodem pós procedimento cirúrgico.⁴⁵ Estudos prospectivos, por sua vez, mostram que esse curso é incomum.⁴⁴ Observações da minha prática clínica que impulsionaram as hipóteses deste trabalho, fazem-me concordar com o grupo que acredita que comportamentos espectrais, tais como agitação motora, eloquência, exuberância na apresentação e muitas vezes condutas agressivas, podem ser sintomas bipolares que eclodem, ou se agravam após a cirurgia.⁴² Desta forma, avaliar um paciente candidato a cirurgia bariátrica, requer muito cuidado e “flexibilidade conceitual”, ou seja, independentemente da credibilidade, da existência da forma espectral pré-cirúrgica, o transtorno bipolar não pode ser subestimado. É necessário ter em mente que este paciente é comórbido e que o transtorno bipolar está dentre as comorbidades mais graves e incapacitantes e associado a outros transtornos, podendo levar ao insucesso do procedimento cirúrgico.

Deste modo, a principal contribuição deste primeiro artigo foi introduzir especificidades dos transtornos psiquiátricos na população com obesidade. Os transtornos de ansiedade, seu curso persistente e sua associação a outras condições psiquiátricas foram o primeiro destaque.¹⁰³ Os transtornos bipolares, como o grupo mais comórbidos, foram o segundo ponto. A comorbidade psicopatológica do paciente com obesidade é um fator agravante que afeta tanto o procedimento clínico, como diretamente a qualidade de vida do paciente. Assim, atenuar os sintomas de ansiedade

persistentes e controlar o transtorno bipolar surge como um alvo clínico relevante a ser considerado durante o período pré e pós-operatório.

6. 2. – Artigo 2

Gender-related patterns of psychiatric disorder clustering among bariatric surgery candidates: a latent class analysis. Duarte-Guerra, L.S.; Coêlho, B.M.; Santo, M.A.; Lotufo-Neto, F.; Wang, Y.P. *Journal Affective Disorders*. 240 (2018) 72-78. doi:10.1016/j.jad. 2018.07.036. Epub 2018 Jul 17.

Permission for reuse by Journal Affective Disorders from Elsevier and Copyright Clearance Center.

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Gender-related patterns of psychiatric disorder clustering among bariatric surgery candidates: A latent class analysis

Leorides Severo Duarte-Guerra^{a,b}, Bruno Mendonça Coêlho^a, Marco Aurélio Santo^c,
Francisco Lotufo-Neto^b, Yuan-Pang Wang^{a,*}

^a Instituto de Psiquiatria (LIM-23), Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil

^b Departamento de Psiquiatria, Faculdade de Medicina FMUSP, Universidade de São Paulo, São Paulo, Brazil

^c Departamento de Cirurgia, Faculdade de Medicina FMUSP, Universidade de São Paulo, São Paulo, Brazil

ARTICLE INFO

Keywords:

Psychiatric disorders
Obesity
Comorbidity
Latent class analysis
Bipolar disorders
Bariatric surgery

ABSTRACT

Background: Psychiatric disorders tend to distribute unevenly in women and men with severe obesity. The current research aimed to identify homogeneous clusters of concurrent psychiatric disorders among patients seeking bariatric surgery, by gender.

Methods: We recruited a consecutive sample of 393 candidates with obesity (311 women and 82 men) in a university-based bariatric center. Trained clinicians assessed psychiatric disorders through the Structured Clinical Interview for DSM-IV (SCID). Latent class analysis categorized pre-surgical patients into uniform clusters of co-occurring psychiatric disorders.

Results: For both genders, the 3-class psychopathological clustering was the best-fitting solution. Among women, the latent classes were: (1) “oligosymptomatic”, wherein 42% of patients showed low probability of psychiatric disorders; (2) “bipolar with comorbidities”, in 33%; and (3) “anxiety/depression”, in 25%. Among men, (1) “bipolar with comorbidities” was found in 47% of patients; (2) “oligosymptomatic”, in 40%; and (3) “anxiety/depression”, in 13%. For both genders, the probability of presenting eating disorders was higher in both “bipolar” and “anxiety/depression” classes. Substance use disorders was prominent among “bipolar” men. In comparison with “oligosymptomatic” class, the likelihood of higher BMI was observed among “bipolar” men and poorer work attainment among men with “anxiety/depression”.

Limitation: Participants was cross-sectionally drawn from a single bariatric center.

Conclusions: Pre-surgical men and women with severe obesity were distributed in three comorbidity profiles and revealed analogous psychopathological patterns. The class of “bipolar disorders” most likely presented comorbidity with eating and substance use disorder. This natural clustering of psychiatric disorders among bariatric patients suggests gender-related therapeutic approaches and surgical outcomes.

1. Introduction

Psychiatric disorders are frequent conditions among persons with obesity (Rajan and Menon, 2017; Schmidt et al., 2011). In general population, obesity and psychiatric disorders affect about 12% and 30% of adult individuals, respectively (NCD Risk factor Collaboration, 2017; GBD 2015 Obesity Collaborators, 2017; Andrade et al., 2012; Kessler et al., 2005). In U.S. general population with obesity, there is around 25% of increase in odds of mood and anxiety disorders and 25% of decrease in odds of substance use disorders (Simon et al., 2006). Therefore, the understanding of the association between obesity and psychiatric disorders may have implications for reduction of burden of

these widespread conditions, in terms of etiology and therapeutics.

In the past decade, bariatric procedures have been popularized as an intervention for those patients with high body-mass index (BMI) that did not respond to conventional pharmacological treatment and changes in life style. For those high-BMI patients seeking bariatric surgery, between 36% and 89% of them meet some criteria for psychiatric disorders (Dawes et al., 2016; Duarte-Guerra et al., 2015; Malik et al., 2014; Lin et al., 2013; Mühlhans et al., 2009; Mauri et al., 2008; Kalarchian et al., 2007). However, most of the studies have investigated the contribution of single mental disorder, in both pre-surgical and post-surgical period. Few health-care professionals are aware of frequent comorbidity of depressive, bipolar, anxiety, eating, and substance

* Corresponding author.

E-mail address: gnap_inbox@hotmail.com (Y.-P. Wang).

<https://doi.org/10.1016/j.jad.2018.07.036>

Received 24 March 2018; Received in revised form 31 May 2018; Accepted 14 July 2018

Available online 17 July 2018

0165-0327/ © 2018 Elsevier B.V. All rights reserved.

use disorders in population with obesity (Apovian et al., 2015). About two-third of patients seeking bariatric surgery present two or more concurrent psychiatric disorders (Duarte-Guerra et al., 2017; Mitchell et al., 2012). Therefore, psychopathological comorbidity seems to be more rule than exception among bariatric patients. The contribution of mental disorders in every stage of bariatric surgery only can be glimpsed when the pattern of comorbidity is taken into account.

The societal pressure on body shape for both men and women, as well as the frequency of psychiatric disorders, is often pointed out as conspicuous contributing factor to differential patterns of comorbidities in the community, (Tronieri et al., 2017; Baskaran et al., 2014). A large community study from the National Epidemiological Study of Alcohol and Related Conditions (NESARC) found association between obesity (BMI > 30) and depressive and anxiety disorders in both sexes (Barry et al., 2008). Similarly, eating disorders seems to affect men and women with obesity in comparable proportion (Tronieri et al., 2017; Mitchell et al., 2015; Desai et al., 2009). Regarding bipolar disorders, most studies from literature have indicated that community-dwelling women present higher risk of obesity than men (Baskaran et al., 2014; Barry et al., 2008). Differently, obesity was associated with increased risk for lifetime alcohol abuse and dependence in men, but not in women (Barry and Petry, 2009). However, no consistent association was found between BMI and illicit drug use, for both genders. In bariatric settings, the relationship between the majority of the psychiatric disorders and obesity is complex and can be further modified by psychosocial variables and treatment settings (Mahony, 2008). The connection between gender, obesity and mental disorders is poorly understood in bariatric settings. As such, investigations on pattern of comorbidity in clinical samples of treatment seeking patients with obesity are mandatory.

The latent class analysis (LCA) is a statistical method of finite mixture modeling to identify subtypes of cases with similar observed categorical data (e.g., psychiatric disorders). These non-observable subtypes or “latent classes” (LC) categorize homogeneous clusters of individuals with shared common characteristics. In other words, a LC reveals the chance that a set of observed variables takes on certain values in a sample of patients. The LC modeling has been widely applied in general population for describing profiles of psychiatric comorbidity (Minihan et al., 2018; Edgcomb and Kerner, 2017; Veltman et al., 2017; Alexandrino-Silva et al., 2013; Kessler et al., 2005; Sullivan et al., 1998). To our knowledge, the patterns of psychopathological comorbidity were rarely investigated among high-BMI bariatric surgery candidates. Previous attempts to describe psychopathological profiles in patients with obesity have examined adolescent sample (Sysko et al., 2011) or through cluster analysis (Martínez et al., 2013).

Clinical identification of meaningful clusters of the psychopathological profiles among patients undertaking bariatric surgery may recommend potential interventions in both pre-surgical phase and predict follow-up outcomes. For example, stable patients with multiple disorders need be properly treated before undertaking surgery. Potential role of percentage of excessive weight loss (%EWL) and quality of life during post-surgery follow-up also needs be established. Distinctive psychopathological patterns by gender in bariatric samples remain sparse and few data have indicated distinct patterns of psychopathological profiles.

By the means of LCA, the aims of current investigation were (a) to examine the comorbidity profile of psychiatric disorders in a sample of pre-surgical patients with class III obesity from the waiting list of gastroplastic procedure; and (b) to determine the associated variables to each identified profile. The clusters of psychiatric disorders among a sample of candidates seeking bariatric surgery were estimated by gender.

2. Material and methods

This is a cross-sectional study for investigating the natural clustering

of psychiatric disorders among treatment-seeking bariatric patients, whose psychopathology was systematically assessed through the Structured Clinical Interview for DSM-IV (Duarte-Guerra et al., 2015). The method of LCA determined possible patterns of psychopathological profiles.

2.1. Sampling

The participants were recruited from the waiting list of a university-based bariatric center in Brazil. The inclusion criteria for the surgery program were: BMI ≥ 40 kg/m², be aged ≥ 18 years, and able to understand the risk/benefit of surgery. The exclusion criteria were: psychosis, intellectual disability, language difficulties, mobility/geographic problems, and previous bypass surgery.

We estimated as an appropriate sample size based on previous report of 66.3% for any Axis I lifetime psychiatric disorders (Kalarchian et al., 2007) in bariatric surgery candidates assessed using SCID interviews. This sample size was estimated to calculate the outcome assessment using simple random sampling to evaluate categorical psychiatric disorders in patients recruited from pre-surgical waiting list. We considered confidence level 95% and precision of 2.2% (standard error) for a finite population and yielded a sample of 471 subjects. Projecting potential participation refusals, we considered the sample size of 500 as acceptable initial number of patients to contact. The sample calculation was performed through the sample size calculator available at National Statistical Service (<http://www.nss.gov.au>). From the first 500 eligible patients to bariatric surgery, 393 individuals accepted to be clinically interviewed in present investigation. The overall participation rate was 78.6%.

Table 1 depicts the demographic characteristics of the sample. Most of the participants were women (79.1%) and mean age of 43.0 years (standard deviation [SD] 11.5). The majority was married/cohabiting (51.1%) and one-quarter was single. The mean years of education were 9.6 (SD 3.6). The mean BMI was 47.8 kg/m² (SD 7.5; range 31.2–92.1), being men's BMI higher than women's index (BMI 50.2 vs. 46.4; $p = 0.01$).

2.2. Assessment of psychiatric disorders

The diagnosis of psychiatric disorders, according DSM-IV (American Psychiatric Association, 2000), was ascertained through the Structured Clinical Interviews for Axis I Disorder – SCID-I (First et al., 2002). The SCID-I provides diagnosis of disorders for current and lifetime period. Six trained clinical psychologists applied the

Table 1
Socio-demographic characteristics of bariatric surgery candidates ($N = 393$).

Variable	N	(%)
Sex		
Female	311	(79.1)
Male	82	(20.9)
Age (mean years, SD)	43.0	(11.5)
Marital status		
Married	201	(51.1)
Single	100	(25.4)
Separated/divorced	65	(16.5)
Widowed	26	(6.6)
Education		
1–8 years	138	(35.1)
9–12 years	175	(44.5)
> 12 years	80	(20.4)
Employment		
Employed	246	(62.6)
Unemployed	147	(37.4)
BMI (mean kg/m², SD)	47.8	(7.5)

BMI: body mass index

SD: standard deviation

interviews after standard course and a 60 h calibration practice. The kappa coefficient for the lifetime psychiatric disorders was 0.81, indicating good pairwise inter-rater agreement. Thereafter, 500 eligible patients were consecutively contacted by phone and randomly assigned to be face-to-face assessed from November 2010 to March 2012.

2.3. Ethical statement

The ethics committee of the University of São Paulo Medical School approved the study. All participants have signed an informed consent before entering the study and were assured that information provided for research would not influence their eligibility for surgery.

2.4. Statistical analysis

The method of latent class analysis (LCA) was used to identify the occurrence of possible of psychiatric disorders classes among candidates for bariatric surgery (Lazarsfeld and Henry, 1968). LCA can be considered as the qualitative version of factor analysis (FA), allows the identification of latent (unobservable) variables from two or more nominal/ordinal (observable) variables (Green 1952, 1951). Preliminary analyses of the frequencies and correlation between DSM-IV diagnostic categories (Table S1) determined the inclusion of observed categorical variables (psychiatric disorders). For the purpose of data analyses, bipolar I, II and not otherwise specified (NOS) disorders were grouped as 'bipolar disorders'; major depression, minor depression and dysthymia as 'depressive disorders'; panic, agoraphobia, social phobia, specific phobia, obsessive-compulsive disorder, post-traumatic stress disorder, generalized anxiety and anxiety NOS as 'anxiety disorders'; use and dependence on alcohol and drugs as 'substance use disorders'; bulimia and binge eating disorder as 'eating disorders'. This initial analysis also revealed that lifetime disorders presented significant tetrachoric correlation in most pairs of disorders (Duarte-Guerra et al., 2017), indicating that the disorders might be clustered in regular patterns of comorbidity in the sample.

Two parameters depicted the model: (1) the prevalence of each latent class and (2) the conditional probability of response in the class. The first parameter describes the distribution of latent classes in the sample, indicating whether the population was equally distributed throughout the classes or if there was any class that stood out over the others. The second parameter represents the probability that a patient in a given LC will give a specific response. The conditional probability represents the chances of a patient of a given class presenting the same psychiatric disorders, in order to demonstrate that each LC is internally homogeneous. These parameters assist the interpretation and identification of the label of LC.

The assumption of LCA was checked for local independence, what has indicated that the occurrence of a particular psychiatric disorder is not associated with the occurrence of another psychiatric disorder within a given class. Thereafter, the SCID-based lifetime disorders of subsample were analyzed through LCA, from two to five classes. This assumption was evaluated by the means of bivariate conditional residues (Agresti, 2002; Haberman, 1973). Residue values greater than 1.96 indicate a potential violation of the assumption of local independence.

Models with different numbers of classes are adjusted and these are compared according to model adjustment statistics and fitness statistical tests. The decision of the final number of LC was based on the Akaike's information criteria (AIC), the Bayesian information criterion (BIC), and the adjusted Bayesian information criterion (aBIC) (Lo et al., 2001; Vuong, 1989). Measures of entropy, Vuong-Lo-Mendell-Rubin (VLMR) likelihood ratio test and the Lo-Mendell-Rubin (LMR) likelihood ratio test complemented the model assessment. To evaluate the magnitude of the reduction of the value of the determinant criterion, the percentage variation between the calculated criteria for the models with k and $k-1$ classes, respectively, was used.

Multiple-group LCA in the total sample was fitted to examine the possibility of a model assuming different psychopathological classes across the men and women's sub-groups. Considering dissimilar frequency of psychiatric disorders between genders (Duarte-Guerra et al., 2015), the separate data of each gender fitted significantly better than the single model. The best model for both women and men was a 3-class solution. This decision was supported by clinical interpretability of the solution and high entropy values (0.80/0.91). The *knownclass* command in Mplus software was introduced to fit the data of 311 women and 82 men.

Taking the less symptomatic LCA as reference, multinomial logistic regression was adjusted to verify the effects of covariates. The following demographic variables: age (years), schooling (years), marital status (married/cohabiting, separated/divorced, single, widowed), BMI (kg/m²), and employment status (working, unemployed), were stepwise entered in the model. For marital status and occupation, the categories "married", and "working" were respectively chosen as reference categories. Education, age, and BMI were entered in the model as continuous variables. Every time a new covariate was entered into the model, the model adjustment was determined.

The analyses were performed through Mplus 6.12 (Muthén and Muthén, 1998–2010) software version 5 (www.statmodel.com) and R version 3.2.1 (www.cran.org). The level of assumed significance was $p < 0.05$, for two-tailed tests.

3. Results

The frequency the DSM-IV psychiatric disorders at the moment of interview was: 46.3% of participants met the criteria for anxiety disorders, 20.1% eating disorders, 13.7% bipolar disorders, 7.9% major depressive disorders, and 3.1% substance use disorders. For lifetime rates, 54.7% of the sample met the criteria for anxiety disorders, 35.6% bipolar disorders, 35.1% eating disorders, 29.3% depressive disorders, and 17.6% substance use disorders. Men presented higher rates of lifetime substance use disorders than women, as well as lifetime bipolar disorder (Fig. 1).

Table 2 displays the adjustment statistics adopted to select the number of LC for women and men, respectively. In both genders the models presented entropy values greater than 0.8 and the 3-class model was the only one that presented substantial change in aBIC value from 2-class or 4-class solution. The likelihood ratio tests also indicated that the 3-class model should be preferred when compared to another model. Therefore, the model with 3 classes for both genders was the best-fitting clustering pattern to the data.

Table 3 shows the conditional probability of frequencies of each psychiatric disorder according to the LC. Patients in each one of retained classes were classified based on *a posteriori* conditional probabilities estimated by the model. The best profile of the LCA solution for women was: class 1, which included 42% of female sub-group, was labeled "oligosymptomatic" because patients in this class have presented low or null probabilities of some psychiatric disorders. Class 2 was called as "bipolar comorbidities", included 33% of women, and was characterized by high rates bipolar and anxiety disorders. Class 3 was named as "anxiety/depression", included 25% of women, and was characterized by high rates of anxiety and depressive disorders.

The best LCA model for men was also a 3-class solution. The first class, with 47% of male sub-group, was called "bipolar comorbidities" because of high rate of bipolar disorders, substance use disorders and anxiety disorders. Class 2 included 40% of men, and was named as "oligosymptomatic" because the patients in this class had low or null probabilities of psychiatric disorder. Class 3 included 13% of men, was labeled as "anxiety/depression", and was composed by high rates of anxiety and depression disorders. Similar best LC profiles are shown in Fig. 2, by gender.

Table 4 showed the results of the effects of covariates by multinomial logistic regression, separated by gender. The covariates, one by

Fig. 1. Comparison of proportion of psychiatric disorders between women and men with severe obesity: (A) current disorders; (B) lifetime disorders.

Table 2
Adjustment parameters of latent class models, by gender.

Number of classes	AIC	BIC	aBIC	Entropy	p-value VLMR	p-value LMR
Women (n = 311)						
2	1698.5	1739.6	1704.7	1.00	< 0.001	< 0.001
3	1671.9	1735.4	1681.5	0.80	< 0.001	< 0.001
4	1677.3	1763.3	1690.4	0.81	0.0397	0.044
5	1689.1	1797.5	1705.6	0.83	0.1974	0.208
Men (n = 82)						
2	493.2	519.7	485.0	0.95	< 0.001	< 0.001
3	484.9	525.8	472.2	0.91	< 0.001	< 0.001
4	492.5	547.9	475.3	0.85	0.117	0.126
5	503.2	573.0	481.5	0.87	0.628	0.633

AIC: Akaike's information criteria

BIC: Bayesian information criterion

aBIC: adjusted Bayesian information criterion

VLMR: Vuong-Lo-Mendell-Rubin likelihood ratio test

LMR: Lo-Mendell-Rubin likelihood ratio test

one, were included in the LC of baseline model. The BMI and unemployment were the only covariates that remained significant for men in the final model. For interpretation, increasing one unit in BMI increases the chance of belonging to the "bipolar comorbidities" class. With regard to occupational status, being unemployed increased the chance of belonging to the "anxiety/depression" class.

4. Discussion

To our knowledge, this is the first time that psychopathological profiles of psychiatric disorders among pre-surgical adult candidates to bariatric surgery were investigated through the technique of LCA. Some strengths of this paper comprise its methods, where SCID-derived psychiatric diagnoses were obtained in a sample of high-BMI patients of

adequate sample size. After appropriate execution of LCA for examining the pattern of comorbidity, we demonstrated that there exist different clustering patterns of psychopathology by gender. Three profiles of patients were found: the 'oligosymptomatic', the 'bipolar with comorbidity', and the 'anxiety/depression' class. The clinical relevance of these psychopathological profiles relies on the possibility of tailoring preventive measures in the pre-surgical period, and investigating the percentage of excessive weight loss and quality of life in the post-bariatric follow-up. Because the distribution of psychopathological clustering was dissimilar among men and women, the gender-focused program may be necessary to address each group of patients with severe obesity.

Psychiatric disorders are common conditions among patients seeking for bariatric surgery (Dawes et al., 2016; Lin et al., 2013; Mühlhans et al., 2009). However, most literature focused on severe obesity has reported the psychopathology as single psychiatric disorders. In the Longitudinal Assessment of Bariatric Surgery (LABS-3) consortium, 68.8% of participants (n = 199) presented at least one lifetime Axis I disorder (Mitchell et al., 2012). The same group also concluded that there is several factors associated with binge eating disorder and suggested the presence of other associated mental health problems, including higher levels of depressive symptomatology (Mitchell et al., 2015).

Furthermore, mood, anxiety, eating, and substance use disorders were found to be present in remarkable patterns of comorbidity and persistence (Duarte-Guerra et al., 2017). This psychopathological pattern may suggest the prognosis of pre-operative psychiatric disorders on later surgical outcome (Burgmer et al., 2014; de Zwaan et al., 2011).

Bearing in mind the possibility of preoperative intervention, we have identified mutually exclusive groups of patients with psychiatric comorbidity, through the technique of LCA. For women, the 'oligo-symptomatic' class was the most frequent profile (42%), followed by 'bipolar' and 'anxiety/depression' class. For men, almost half were

Table 3
Best-fitting conditional probability of the frequency of psychiatric disorders in each class, by gender.

Disorders	Classes of women (n = 311)				Classes of men (n = 82)			
	Oligo-symptomatic n (%)	Bipolar comorbidities n (%)	Anxiety & depression n (%)	N (%)	Oligo-symptomatic n (%)	Bipolar comorbidities n (%)	Anxiety & depression n (%)	N (%)
Bipolar disorder	0 (0)	103 (100)	0 (0)	103 (33)	0 (0)	37 (97)	0 (0)	37 (45)
Anxiety disorder	25 (19)	76 (74)	76 (99)	177 (57)	4 (12)	23 (61)	11 (100)	38 (46)
Depressive disorder	32 (24)	0 (0)	65 (84)	97 (31)	7 (21)	0 (0)	11 (100)	18 (22)
Eating disorder	22 (17)	51 (50)	36 (47)	109 (35)	4 (12)	19 (50)	6 (55)	29 (35)
Substance use disorder	0 (0)	30 (29)	9 (12)	39 (13)	6 (18)	24 (63)	0 (0)	30 (37)
Total	131 (42)	103 (33)	77 (25)	311 (100)	33 (40)	38 (47)	11 (13)	82 (100)

Fig. 2. Best-fitting latent class model of psychiatric disorders in patients with severe obesity: (A) women; (B) men.

clustered in the class of 'bipolar comorbidities'; followed by 'oligo-symptomatic' and 'anxiety/depression' class. For both genders, eating disorders were a frequent condition in around half of patients in both 'bipolar' and 'anxiety/depression' class. The women/men ratio of substance use disorders was around 1:2 in the 'bipolar' class (Diflorio and Jones, 2010; Albanese et al., 2006).

According to Segura-Garcia et al. (2017), binge eating disorder and bipolar spectrum are common comorbid disorders in a sample of patients with obesity. The authors have highlighted the association of this double comorbidity to more severe psychopathology and eating behaviors in obesity. Therefore, the distinctive psychopathological pattern of comorbidity must be considered during all phases of evaluation in bariatric surgery.

In non-clinical settings, several studies have demonstrated distinctive symptomatic patterns of psychiatric disorders through LCA. For example, among six subtypes of depressive disorder in U.S. general population, symptoms of increased appetite and weight gain prevailed in the class of atypical depression (Sullivan et al., 1998). Furthermore, Kessler et al. (2005) described seven non-overlapping classes of comorbidity using U.S. data from the National Comorbidity Survey – Replication. Three highly comorbid classes encompassed 7% of the sample, where the most serious cases were concentrated. The bipolar class was the most comorbid and severe class.

Among patients with obesity, the method of LCA has explored eating disorders phenotypes (Swanson et al., 2014; Wade et al., 2006) and temperament traits of pre-bariatric patients (Schafer et al., 2017). Sysko et al. (2011) identified a 3-class solution of psychiatric symptoms among 125 adolescents attending a bariatric program. The profiles were eating disorders with comorbidity, low psychopathology, and non-specific psychopathology. While heterogeneous levels of

psychopathologies were highlighted in terms of severity, distinctive types of psychopathologies remained elusive. Using cluster analysis, Martínez et al. (2013) also have identified three separate symptomatic subgroups in 50 pre-bariatric adult patients. Similarly to our findings, the bipolar group stood out. Beside different sample characteristics (e.g., age and sample size), these two studies have assessed the key psychopathology through self-report instruments.

Gender difference in psychopathological disorder patterns was already well documented in general population (Alexandrino-Silva et al., 2013; Kessler et al., 1994). Biological sexual determinants of mental health are conspicuous explanation for heterogeneous psychopathologies. However, gender-related determinants also contribute saliently to disease risks to men and women. Different gender-specific roles, socio-occupational competition in the labor market, help-seeking behavior, and aesthetic demands are some potential contributors to this scenario (World Health Organization, 2017). Regarding psychopathology, we are not able to find out any study exploring gender difference of psychiatric comorbidity in bariatric samples.

In our study, the LCA models identified that there exist homogeneous profiles of women and men, regarding BMI, psychopathological distributions and help-seeking behavior to bariatric surgery. Although both groups presented similar patterns of comorbidities, men tended to cluster in more severe class of 'bipolar disorder with comorbidity'. Conversely, women presented more 'anxiety/depression' than men. Furthermore, eating disorders contributed substantially to both 'bipolar' and 'anxiety/depression' class in both genders. While the literature confirms that substance use disorders prevailed among 'bipolar' men (Diflorio and Jones, 2010), the substance use was observed among 'anxiety/depression' women in our sample. Even most epidemiological studies has reported that obesity was more associated in

Table 4

Multinomial logistic regression of determinants of latent class model, by gender.

	Women (n = 311)						Men (n = 82)					
	Bipolar comorbidities*			Anxiety & Depression*			Bipolar comorbidities*			Anxiety & Depression*		
	OR	IC (95%)	p	OR	IC (95%)	p	OR	IC (95%)	p	OR	IC (95%)	p
Marital status												
Married/cohabiting	1.00			1.00			1.00			1.00		
Widowed	1.09	0.27	4.34	0.904	2.80	0.66	11.96	0.165	–	–	–	–
Separated/divorced	1.30	0.56	3.01	0.542	1.25	0.39	3.98	0.711	0.97	0.21	4.57	0.967
Single	1.02	0.51	2.03	0.960	0.79	0.29	2.14	0.649	3.13	0.92	10.63	0.067
Education (years)	0.96	0.88	1.04	0.290	0.98	0.87	1.10	0.669	0.91	0.77	1.06	0.225
Age (years)	0.98	0.96	1.01	0.226	0.98	0.95	1.02	0.283	1.00	0.96	1.04	0.966
BMI (kg/m²)	0.98	0.93	1.02	0.288	1.01	0.95	1.09	0.675	1.07	1.01	1.14	0.022
Employment												
Employed	1.00			1.00			1.00			1.00		
Unemployed	0.65	0.36	1.17	0.152	0.63	0.28	1.45	0.278	1.25	0.37	4.22	0.719
										5.09	1.25	20.68
												0.023

* Oligosymptomatic class is the reference group.

women than men (Baskaran et al., 2014; Barry et al., 2008), participation bias may have selected more severe men than women in the present study. For example, treatment-seeking bipolar men in the bariatric setting used to present higher BMI than women (Mahony, 2008), and were associated to poorer working attainment. This gender-related psychopathological profile suggests a number of avenues for future research.

4.1. Limitations

Before extending our findings to other patients seeking bariatric surgery, we should bear in mind some limitations. Our sample of patients was drawn from a single bariatric center. Therefore, the sample may be prone to selection bias, which findings may not be generalized to other bariatric samples or patients with obesity. Notwithstanding, the sample size of our study was adequate to implement the multivariate analysis.

The cross-sectional nature of the design did not allow predicting post-surgical outcome, in terms of percentage of excessive weight loss (%EWL), control of metabolic parameters, psychopathology, and quality of life. Prospective and case-control designs are warranted to confirm the utility of therapeutic intervention of the sub-group of patients in the pre-surgical period.

5. Comments

Psychiatric disorders are long-lasting conditions among high-BMI candidates searching bariatric surgery. The current latent class analysis has identified heterogeneous subgroups of patients with homogeneous levels of psychopathology among a sample of adults with severe obesity during the pre-surgical period. In comparison with women, men most likely have clustered in the class of ‘bipolar’ disorders associated with comorbid anxiety, eating, and substance use disorders.

Remarkable gender difference in the frequency of the class profiles provides opportunities of prevention, treatment in both pre-surgical and follow-up periods. In the pre-surgical period, the indication to undertake surgery only can take place after stabilization of these psychopathological profiles. In post-surgical period, potential latent disorders can unleash because of surgical procedure. Therefore, the clinician must closely monitor comorbid cases of substance use, self-harm behavior, active phase of mood episode (either depression or manic/hypomanic phase). Future suggested paths that worth further investigation are gender-specific longitudinal evaluation of post-surgical outcome, in terms of excessive weight loss (%EWL), adherence to treatment, quality of life, self-harm behavior, substance use disorder, post-surgical mortality, disability, health service use, etc.

Continuous assessment of patients with obesity undergoing surgery by qualified multidisciplinary team in all phases of the bariatric process is recommended. The clinical impact of these comorbidity profiles must be demonstrated in prospective investigations. To conclude, our study on gender-specific psychopathological profile during pre-operative phase can contribute to grasp the course of obesity, to rethink about when and how clinician may indicate bariatric surgery and treatment of high-BMI patients.

Role of funding source

The investigation received grant from the [Foundation for Research Support of the State of São Paulo](#) (FAPESP # 2012/17,435-7) and Y.-P. W. was the recipient of this grant. The FAPESP supported data collection of this research. This agency had no further influence in study design, in the data collected, the analytical strategy, in the interpretation of data and results reported herein, in the decision to disseminate as article for publication, the writing of the report, and the contents of this article.

Conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Statement of human and animal rights

All procedures involving human participants performed in current study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The ethics committee of the University of São Paulo Medical School approved the study.

Authors contributions

LSDG declares that have participated in the study and my specific contribution as follow: conception and design of the research, acquisition of data, analysis and interpretation of data, statistical analysis, drafting of the manuscript, critical revision of the manuscript for the important intellectual content.

YPW declares that have participated in the study and my specific contribution as follow: conception and design of the research, acquisition of data, analysis and interpretation of data, statistical analysis, drafting of the manuscript, critical revision of the manuscript for the important intellectual content, and supervision as the principal investigator.

BMC declares that have participated in the study and my specific contribution as follow: acquisition of data, critical revision of the manuscript for the important intellectual content.

MAS declares that have participated in the study and my specific contribution as follow: conception and design of the research, acquisition of data, critical revision of the manuscript for the important intellectual content.

FLN declares that have participated in the study and my specific contributions were as follows: conception and design of the research, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for the important intellectual content.

Acknowledgment

L.S.D.G. was awarded with a Masters scholarship from the Foundation for Research Support of the State of São Paulo (FAPESP # 2012/17498-9).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.jad.2018.07.036](https://doi.org/10.1016/j.jad.2018.07.036).

References

- Agresti, A., 2002. *Categorical Data Analysis*, second ed. Wiley Series in Probability and Statistics.
- Albanese, M.J., Clodfelter Jr., R.C., Pardo, T.B., Ghaemi, S.N., 2006. Underdiagnosis of bipolar disorder in men with substance use disorder. *J. Psychiatr. Pract.* 12, 124–127.
- Alexandrino-Silva, C., Wang, Y.P., Viana, M.C., Bulhões, R.S., Martins, S.S., Andrade, L.H., 2013. Gender differences insymptomatic profiles of depression: results from the São Paulo Megacity Mental Health Survey. *J. Affect. Disord.* 147, 355–364.
- American Psychiatric Association, 2000. *Diagnostic and Statistical Manual of Mental Disorders*, fourth ed. American Psychiatric Association, Washington DC.
- Andrade, L.H., Wang, Y.P., Andreoni, S., Silveira, C.M., Alexandrino-Silva, C., Siu, E.R., Nishimura, R., Anthony, J.C., Gattaz, W.F., Kessler, R.C., Viana, M.C., 2012. Mental disorders in megacities: finding from the São Paulo megacity mental health survey,

- Brazil. PLoS One 7, e31879.
- Apovian, C.M., Garvey, W.T., Ryan, D.H., 2015. Challenging obesity: patient, provider, and expert perspectives on the roles of available and emerging nonsurgical therapies. *Obesity* 22, S1–S26.
- Barry, D., Petry, N.M., 2009. Associations between body mass index and substance use disorders differ by gender: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Addict. Behav.* 34, 51–60.
- Barry, D., Pietrzak, R.H., Petry, N.M., 2008. Gender differences in associations between body mass index and DSM-IV mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Ann. Epidemiol.* 18, 458–466.
- Baskaran, A., Cha, D.S., Powell, A.M., Jalil, D., McIntyre, R.S., 2014. Sex differences in rates of obesity in bipolar disorder: postulated mechanisms. *Bipolar Disord.* 16, 83–92.
- Burgmer, R., Legenbauer, T., Müller, A., de Zwaan, M., Fischer, C., Herpertz, S., 2014. Psychological outcome 4 years after restrictive bariatric surgery. *Obes. Surg.* 24, 1670–1678.
- Dawes, A.J., Maggard-Gibbons, M., Maher, A.R., Booth, M.J., Mlake-Lye, I., Beroes, J.M., Shekelle, P.G., 2016. Mental health conditions among patients seeking and undergoing bariatric surgery: a meta-analysis. *JAMA* 315, 150–163.
- de Zwaan, M., Enderle, J., Wagner, S., Mühlhans, B., Ditzel, B., Gefeller, O., Mitchell, J.E., Müller, A., 2011. Anxiety and depression in bariatric surgery patients: a prospective, follow-up study using structured clinical interviews. *J. Affect. Disord.* 133, 61–68.
- Desai, R.A., Manley, M., Desai, M.M., Potenza, L.M., 2009. Gender differences in the association between body mass index and psychopathology. *CNS Spectr.* 14, 372–383.
- Diforio, A., Jones, L., 2010. Is sex important? Gender differences in bipolar disorder. *Int. Rev. Psychiatry* 22, 437–452.
- Duarte-Guerra, L.S., Coelho, B.M., Santo, M.A., Wang, Y.P., 2015. Psychiatric disorders among obese patients seeking bariatric surgery: results of structured clinical interviews. *Obes. Surg.* 25, 830–837.
- Duarte-Guerra, L.S., Coelho, B.M., Santo, M.A., Lotufo-Neto, F., Wang, Y.P., 2017. Morbidity persistence and comorbidity of mood, anxiety, and eating disorders among preoperative bariatric patients. *Psychiatry Res* 257, 1–6.
- Edgcomb, J.B., Kerner, B., 2017. Predictors and outcomes of somatization in bipolar I disorder: A latent class mixture modeling approach. *J. Affect. Disord.* 227, 681–687.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 2002. Structured Clinical Interview For DSM-IV-TR Axis I Disorders. Biometrics Research: New York State Psychiatric Institute, New York Research Version, Patient Edition. (SCID-I/P).
- GBD 2015 Obesity Collaborators, 2017. Health effects of overweight and obesity in 195 countries over 25 years. *N. Engl. J. Med.* 377, 13–27.
- Green, B.F., 1951. A general solution for the latent class model of latent structure analysis. *Psychometrika* 16, 151–166.
- Green, B.F., 1952. Latent structure analysis and its relation to factor analysis. *J. Am. Stat. Assoc.* 47, 71–76.
- Haberman, S.J., 1973. The analysis of residuals in cross-classified tables. *Biometrics* 29, 205–220.
- Kalarchian, M.A., Marcus, M.D., Levine, M.D., Courcoulas, A.P., Pilkonis, P.A., Ringham, R.M., Soukova, J.N., Weissfeld, L.A., Rofey, D.L., 2007. Psychiatric disorders among bariatric surgery candidates: relationship to obesity and functional health status. *Am. J. Psychiatry* 164, 328–334.
- Kessler, R.C., Chiu, W.T., Demler, O., Merikangas, K.R., Walters, E.E., 2005. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCSR). *Arch. Gen. Psychiatry* 62, 617–627.
- Kessler, R.C., McGonagle, K.A., Nelson, C.B., Hughes, M., Swartz, M., Blazer, D.G., 1994. Sex and depression in the National Comorbidity Survey II: cohort effects. *J. Affect. Disord.* 30, 15–26.
- Lazarsfeld, P., Henry, N., 1968. Latent Structure Analyses. Houghton-Mifflin, Boston.
- Lin, H.Y., Huang, C.H., Tai, C.M., Lin, H.Y., Kao, Y.H., Tsai, C.C., Hsuan, C.F., Lee, S.L., Yen, Y.C., 2013. Psychiatric disorders of patients seeking obesity treatment. *BMC Psychiatry* 13, 1.
- Lo, Y., Mendell, N., Rubin, D., 2001. Testing the number of components in a normal mixture. *Biometrika* 88, 767–778.
- Mahony, D., 2008. Psychological gender differences in bariatric surgery candidates. *Obes. Surg.* 18, 607–610.
- Malik, S., Mitchell, J.E., Engel, S., Crosby, R., Wonderlich, S., 2014. Psychopathology in bariatric surgery candidates: a review of studies using structured diagnostic interviews. *Compr. Psychiatry* 55, 248–259.
- Martínez, E.P., González, S.T., Vicente, M.M., van der Hofstadt Roman, C.J., Rodríguez-Marin, J., 2013. Psychopathology in a sample of candidate patients for bariatric surgery. *Int. J. Psychiatry Clin. Pract.* 17, 197–205.
- Mauri, M., Rucci, P., Calderone, A., Santini, F., Oppo, A., Romano, A., Rinaldi, S., Armani, A., Polini, M., Pinchera, A., Cassano, G.B., 2008. Axis I and II disorders and quality of life in bariatric surgery candidates. *J. Clin. Psychiatry* 69, 295–301.
- Mitchell, J.E., Selzer, F., Kalarchian, M.A., Devlin, M.J., Strain, G., Elder, K.A., Marcus, M.D., Wonderlich, S., Christian, N.J., Yanovski, S.Z., 2012. Psychopathology prior to surgery in the Longitudinal Assessment of Bariatric Surgery-3 (LABS-3) psychosocial study. *Surg. Obes. Relat. Dis.* 8, 533–541.
- Mitchell, J.E., King, W.C., Courcoulas, A., Dakin, G., Elder, K., Engel, S., Flum, D., Kalarchian, M., Khandelwal, S., Pender, J., Pories, W., Wolfe, B., 2015. Eating behavior and eating disorders in adults before bariatric surgery. *Int. J. Eat. Disord.* 48, 215–222.
- Minihan, S., Liddell, B.J., Byrow, Y., Bryant, R.A., Nickerson, A., 2018. Patterns and predictors of posttraumatic stress disorder in refugees: a latent class analysis. *J. Affect. Disord.* 232, 252–259.
- Mühlhans, B., Horbach, T., de Zwaan, M., 2009. Psychiatric disorders in bariatric surgery candidates: a review of the literature and results of a German prebariatric surgery sample. *Gen. Hosp. Psychiatry* 31, 414–421.
- Muthén, L., Muthén, B., 1998. Mplus User's Guide. Muthén & Muthén, Los Angeles, CA.
- NCD Risk Factor Collaboration (NCD-RisC), 2017. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 390, 2627–2642.
- Rajan, T.M., Menon, V., 2017. Psychiatric disorders and obesity: a review of association studies. *J. Postgrad. Med.* 63, 182–190.
- Schafer, L., Hubner, C., Carus, C., Herbig, B., Seyfried, F., Kaiser, S., Schutz, T., Dietrich, A., Hilbert, A., 2017. Identifying prebariatric subtypes based on temperament traits, emotion dysregulation, and disinhibited eating: a latent profile analysis. *Int. J. Eat. Disord.* 50, 1172–1182.
- Schmidt, M.I., Duncan, B.D., Azevedo e Silva, G., Menezes, A.M., Monteiro, C.A., Barreto, S.M., Chor, D., Menezes, P.R., 2011. Chronic non-communicable diseases in Brazil: burden and current challenges. *Lancet* 377, 1949–1961.
- Segura-Garcia, C., Caroleo, M., Rania, M., Barbuti, E., Sinopoli, F., Aloï, M., Arturi, F., De Fazio, P., 2017. Binge eating disorder and bipolar spectrum disorders in obesity: psychopathological and eating behaviors differences according to comorbidities. *J. Affect. Disord.* 208, 424–430.
- Simon, E.G., Von Korff, M., Saunders, K., Miglioretti, D.L., Crane, P.K., van Belle, G., Kessler, R.C., 2006. Association between obesity and psychiatric disorders in the US adult population. *Arch. Gen. Psychiatry* 63, 824–830.
- Sullivan, P.F., Kessler, R.C., Kendler, K.S., 1998. Latent class analysis of lifetime depressive symptoms in the national comorbidity survey. *Am. J. Psychiatry* 155, 1398–1406.
- Swanson, S.A., Horton, N.J., Crosby, R.D., Micali, N., Sonnevile, K.R., Eddy, K., Field, A.E., 2014. A latent class analysis to empirically describe eating disorders through developmental stages. *Int. J. Eat. Disord.* 47, 762–772.
- Sysko, R., Zakarin, E.B., Devlin, M.J., Bush, J., Walsh, B.T., 2011. A latent class analysis of psychiatric symptoms among 125 Adolescents in a bariatric surgery program. *Int. J. Pediatr. Obes.* 6, 289–297.
- Tronieri, J.S., Wurst, C.M., Pearl, R.L., Allison, K.C., 2017. Sex differences in obesity and mental health. *Curr. Psychiatry Rep.* 19, 29.
- Veltman, E.M., Lamers, F., Comijs, H.C., de Waal, M.W.M., Stek, M.L., van der Mast, R.C., Rhebergen, D., 2017. Depressive subtypes in an elderly cohort identified using latent class analysis. *J. Affect. Disord.* 218, 123–130.
- Vuong, Q.H., 1989. Likelihood ratio tests for model selection and non-nested hypotheses. *Econometrica* 57, 307–333.
- Wade, T.D., Crosby, R.D., Martin, N.G., 2006. Use of latent profile analysis to identify eating disorders phenotypes in an adult Australian twin cohort. *Arch. Gen. Psychiatry* 63, 1377–1384.
- World Health Organization, 2017. Gender and Women's Mental Health (WHO). Gender disparities and Mental health: The Facts. World Health Organization, Geneva [Available at: http://www.who.int/mental_health/prevention/genderwomen/en/; Accessed on February 3, 2018].

4.2.2 – Discussão do artigo 2

O segundo artigo “*Gender-related patterns of psychiatric disorders clustering among bariatric surgery candidates: a latent class analysis*”, investigou os padrões de agrupamento dos transtornos psiquiátricos em pacientes candidatos à cirurgia bariátrica, discriminados por gêneros, e verificou a influência de covariáveis sociodemográficas nos perfis encontrados. Estas análises foram realizadas utilizando os dados ao longo da vida, uma vez que no momento da entrevista muitos transtornos não apareceram, devido a possíveis tratamentos realizados. Apesar de comum acordo na literatura de que mulheres representam as taxas mais frequentes e os homens os IMC mais elevados, a abordagem realizada por separação de gêneros se justifica devido à escassez de estudos que abordam essas diferenças em relação aos padrões dos transtornos psiquiátricos.

Mulheres e homens apresentaram padrões de agrupamentos similares, formaram três classes psicopatológicas, com características semelhantes. A diferença se mostrou na frequência condicional das classes. O subgrupo masculino apresentou maior frequência na classe “bipolar com comorbidades”. Essa classe multicomórbida é grave e coocorre com ansiedade, uso de substâncias e transtornos alimentares. Por outro lado o subgrupo feminino permaneceu com maior frequência na classe “depressiva com ansiedade”, quase o dobro comparado com a masculina. Porém, apesar de enfatizar a gravidade dos homens como tendo os índices de massa corpórea mais elevados, com comorbidades mais graves e incapacitantes, o ponto importante que o estudo apresentou foram os critérios que levaram à formação das classes. Na literatura é consenso que os transtornos alimentares, transtornos de compulsão alimentar (TCA), devem sempre estar em destaque, em pacientes com obesidade grau III.¹⁷ Desta forma, a suposição inicial era encontrar uma classe predominantemente formada por pacientes com TCA. Porém, apesar dos transtornos alimentares serem frequentes em todas as classes, não houve um agrupamento em que os TA fossem o “carro chefe”, ou seja, não encabeçou nenhum conjunto como o transtorno mais relevante. O transtorno bipolar, apesar de não ser o mais frequente, quando ajustado por padrões, tornou-se o mais relevante, destacando que nomeou uma classe: “Bipolar com comorbidades”. O mesmo ocorreu com a classe

“Ansiedade/depressão”. Entendemos que esta classificação de ajustamento dos transtornos se deu pelo critério de gravidade e não pela frequência. Assim, por meio dos método de análise de classe latente, apresentamos uma nova perspectiva para associações entre transtornos psiquiátricos e obesidade, não só pela frequência, mas principalmente pela gravidade das comorbidades.

Outro importante aspecto introduzido neste trabalho está na diferenciação por gênero. As taxas de obesidade são mais frequentes em mulheres, assim como a procura pelo procedimento cirúrgico, porém homens apresentam elevados IMC e transtornos psiquiátricos mais graves, além do resultado da regressão multinomial que mostrou a variável “desocupação” que influencia a formação de classe em homens. A perda da ocupação profissional atinge a saúde mental, levando a transtornos depressivos, condutas antissociais e suicídios.¹⁰⁵ Apesar de alguns estudos começarem a distinguir as diferenças de gênero no cenário bariátrico, os centros de tratamentos de obesidade, com ou sem intervenção cirúrgica, ainda não introduziram abordagens que contemplem estas diferenças entre homens e mulheres.¹⁰⁶

A nova perspectiva de análise da gravidade dos transtornos psiquiátricos e as diferenças entre mulheres e homens, apresentados no presente artigo, poderão orientar toda a equipe multidisciplinar para a avaliação pré-cirúrgica, tratamento e acompanhamento do paciente bariátrico. O uso de metodologia estatística avançada, análise de classe latente, contribuiu tanto com a apresentação dos resultados, bem como a introdução da técnica em si, no conjunto multidisciplinar da cirurgia bariátrica. Apesar de amplamente utilizada nas Ciências Sociais, e agora em pesquisas clínicas, o método de análise de classe latente não tem sido muito divulgado entre as principais revistas dedicadas à cirurgia bariátrica. Desta forma, a apresentação da análise de classe latente e seus resultados na população com obesidade traz novas dimensões as etapas do procedimento cirúrgico. Os transtornos psiquiátricos têm graves implicações durante todas as fases que envolvem a cirurgia bariátrica. No período pré-cirúrgico, a elegibilidade à cirurgia só pode ocorrer após estabilização desses perfis psicopatológicos. No período pós-operatório, potenciais transtornos latentes podem ser desencadeados pelo procedimento cirúrgico, ou os já existentes serem agravados. Portanto, o clínico deve monitorar de perto os casos comórbidos de uso de substâncias e

fases de episódio de humor (depressão ou fase maníaca/hipomaníaca). Deste modo, a principal contribuição deste estudo foi apresentar perfis psicopatológicos de pacientes candidatos à cirurgia bariátrica, reconhecer as diferenças de gêneros no diagnóstico psiquiátrico, e alertar para gravidade dos transtornos bipolares.

5 – Discussão

O interesse em investigar os transtornos psiquiátricos que ocorrem em pacientes candidatos à cirurgia bariátrica surgiu a partir da observação frequente de sintomas maniformes durante o seu atendimento clínico. Ao longo da minha prática privada como psicóloga clínica, múltiplos estágios em ambulatorios psiquiátricos e cirúrgicos, complementados com achados da literatura, algumas particularidades dos pacientes com obesidade chamaram a minha atenção. Os pacientes com obesidade grau III, com regularidade, exibiam comportamentos exuberantes, falavam com eloquência, acompanhados de gesticulações efusivas que excediam o padrão tipo “bonachão” do senso-comum. Cismada com estas observações inusitadas neste grupo de pacientes, planejei um estudo observacional sobre suas características psicopatológicas, cujos dados iniciais permitiram expandir progressivamente a investigação científica dos transtornos psiquiátricos em pacientes com obesidade. Nesta monografia descrevemos o curso, a concomitância e padrão de comorbidade psicopatológica dos pacientes, bem como a influência de gêneros e fatores determinantes.

O primeiro passo foi o levantamento das frequências dos transtornos psiquiátricos entre pacientes candidatos à cirurgia. Rigorosa metodologia garantiu a excelência do estudo e obtivemos uma amostra composta por 393 pacientes candidatos a cirurgia bariátrica; sendo a segunda maior dentre sete estudos semelhantes, que variaram de 86 a 455 participantes.^{17-19,21,24,45,46} Além de amostra de tamanho suficiente, a coleta dos dados foi realizada, por profissionais clínicos treinados, que aplicaram um roteiro de entrevista padronizada (SCID I/P), padrão-ouro em pesquisa. O uso da entrevista padronizada (SCID I/P), que é reproduzível, permitiu extrair diagnósticos psiquiátricos ancorados nos critérios do DSM-IV. A maioria dos estudos em pacientes com obesidade faz uso de escalas diagnósticas ou somente módulos específicos da SCID I/P.⁹¹ De acordo com as referências bibliográficas, esperava-se taxas elevadas de transtornos psiquiátricos nessa população, e de fato, a análise primária dos dados corroborou os estudos existentes.^{17-19,21,24,45,46} Contudo, uma apreciação aprofundada dos resultados encontrados, mostrou que, além de muito frequente, os transtornos psiquiátricos apresentavam particularidades nos padrões psicopatológicos. Desta forma, iniciou-se uma nova fase, por meio das análises secundárias dos dados, com ênfase no foco não nas categorias diagnósticas simples, mas na compreensão do curso,

concomitância e posteriormente possíveis padrões de agrupamentos psicopatológicos entre os pacientes com obesidade que aguardavam o procedimento cirúrgico.

Os resultados de modo geral, foram inesperados. A investigação do curso e coocorrência dos transtornos mostraram os transtornos de ansiedade como os mais persistentes, com elevadas taxas no momento atual e ao longo da vida. A cronicidade dos transtornos de ansiedade foi discutida no primeiro artigo, juntamente com a concomitância de outros transtornos, em que o transtorno bipolar apareceu como o mais comórbido. Esses resultados destacaram os sintomas de ansiedade, que apesar de frequentes, persistentes e muitas vezes com sintomas incapacitantes, não têm sua importância considerada pelos clínicos. Muitas vezes, esses sintomas são vistos como característicos e naturais do paciente com obesidade e não passíveis de tratamento. O transtorno bipolar, por sua vez, foi o transtorno que mais se associou aos demais. Em uma população onde dois terços apresentam dois ou mais transtornos mentais, e o transtorno bipolar sendo o mais comórbido, sugere que este transtorno pode estar muito mais associado à obesidade, do que se tem considerado.

No segundo artigo apresentamos os padrões psicopatológicos encontrados. Esta etapa da investigação foi realizada verificando, também, as diferenças de gênero e fatores sociodemográficos que poderiam estar influenciando a associação dos transtornos mentais em pacientes com obesidade tipo III. Apesar do consenso na literatura afirmar que as taxas de obesidade são mais frequentes em mulheres, e que os homens apresentam os índices de massa corporal mais elevados, há poucos estudos que investigam fatores que influenciam essas diferenças associadas a transtornos mentais. Para essas análises utilizamos estratégias analíticas multivariadas de classe latente. Pesquisas sobre padrões psicopatológicos nesta população já vem sendo realizadas, porém com amostras pequenas e com metodologia que não permitiram resultados conclusivos.^{84,85} O estudo de Sysko e colegas⁸⁴ identificou três subgrupos sintomáticos distintos entre adolescentes candidatos a cirurgia, porém, nesse estudo, além da amostra pequena, a solução final mostrou apenas as diferenças na quantidade de patologias e não em relação aos tipos de patologias. O estudo de Martinez e colegas⁸⁵ utilizou uma metodologia semelhante, a análise de cluster, e também identificou três subgrupos

sintomáticos distintos em adultos, sendo um grupo composto por elevadas taxas de transtorno bipolar.

Desta forma, o presente estudo preencheu uma lacuna, uma vez que utilizou método estatístico apurado que identificou os padrões psicopatológicos entre pacientes pré-cirúrgicos adultos, apresentando tanto o parâmetro da prevalência de cada classe, bem como a probabilidade condicional de solução das classes. As análises destacaram o transtorno bipolar, que pelo critério de gravidade formou uma classe especial com elevada comorbidade, mais frequente em homens e associada ao uso de substâncias, superando os transtornos alimentares. Isto surpreendeu, pois até então a ênfase da literatura foi sobre os transtornos de compulsão alimentar, considerados a principal comorbidade e a mais grave, sendo responsável pelos altos índices de massa corpórea.^{27,59} Nosso estudo, direciona a atenção ao transtorno bipolar que sobressaiu-se como o mais grave. Desconstrói a ideia de que o principal transtorno mental do paciente com obesidade grave é o transtorno de compulsão alimentar. Os achados sugerem que os transtornos do humor e suas alterações neuroquímicas, parecem ter um papel muito mais ativo do que previamente se conhecia,^{107,108} visto que o transtorno bipolar foi colocado em evidência. Desta forma, obesidade pode ser estudada sob uma nova perspectiva, que pode direcionar futuros estudos e ampliar a compreensão da etiologia da obesidade

A obesidade e sua complexa etiologia vêm sendo exploradas há anos e muitas questões ainda permanecem sem respostas. O tratamento cirúrgico surgiu e alcançou em poucos anos índices exponenciais. Este incisivo e drástico procedimento cirúrgico aumentou a complexidade do tratamento da obesidade. Na verdade existem subgrupos de pacientes com comorbidades diferentes e que necessitam de abordagens terapêuticas específicas. Nosso estudo sobre perfis psicopatológicos específicos de acordo com o gênero, durante a fase pré-operatória, representa uma contribuição adicional para compreender o amplo e complexo curso da obesidade e sua relação com os transtornos psiquiátricos. Considero que os resultados dessas análises contribuem para os clínicos reconhecerem os diferentes perfis psicopatológicos entre mulheres e homens e avaliarem com maior precisão a elegibilidade do paciente com índice de massa corporal elevado para a cirurgia bariátrica. Os dados sugerem que homens apresentam as taxas mais elevadas na classe grave “bipolar com comorbidades”, o que deve servir de alerta

tanto para a indicação cirúrgica, como para os tratamentos convencionais. Compreender, ainda, que alguns comportamentos, devem ser vistos com cautela, pois estigmas sobre a conduta “alegre” e “bonachona” desses pacientes podem acobertar sintomas de ansiedade e/ou hipomaníacos.

Finalizando, os resultados das investigações desta tese corroboram as observações que motivaram o início desta pesquisa, sustentam as hipóteses levantadas de que transtornos mentais em pacientes bariátricos são persistentes e comórbidos, que há padrões distintos de psicopatologia que diferenciam homens e mulheres, e ainda há influência de fatores sociodemográficos, como, por exemplo, o desemprego entre homens. Ao meu ver, esses resultados sugerem um questionamento sobre o atendimento do paciente com obesidade, sendo necessário aprofundar os critérios avaliativos para indicação cirúrgica e novos procedimentos no tratamento convencional.

Por sua vez, para apresentação desta tese, optei pelo formato de compilação de artigos publicados, fugindo do modelo tradicional de teses acadêmicas. Este formato além de permitir mostrar os principais resultados sobre as questões investigadas, possibilitou apresentar a produção científica realizada durante o programa de pós-graduação. Os artigos publicados ilustram os passos da construção do pensamento científico que norteou o projeto inicial do mestrado até o presente estudo de doutorado, de forma compacta e já dentro dos moldes exigidos pelas revistas da comunidade científica.

Futuras implicações

O impacto clínico desses perfis de comorbidades deve ser demonstrado em futuras investigações prospectivas. Os caminhos sugeridos que merecem uma investigação mais aprofundada são: avaliação do resultado pós-cirúrgico levando em conta perda excessiva de peso, adesão ao tratamento, qualidade de vida, comportamento autodestrutivo, transtornos por uso de substâncias, mortalidade pós-cirúrgica, incapacitação, uso de serviços de saúde. Avaliação contínua de pacientes com obesidade submetidos à cirurgia por equipe multidisciplinar qualificada em todas as fases do processo bariátrico é recomendada. Análises futuras poderão, talvez, elucidar que o corpo de dimensões desproporcionais pode estar etiológicamente muito mais associado

a aspectos neurobiológicos do transtorno do humor, do que necessariamente em relação ao comer compulsivo.

Limitações

Faz-se importante ressaltar algumas limitações deste trabalho, que nos alertam para possibilidades reais de generalização e validade externa dos resultados. Primeiro, trata-se de uma população clínica, sendo uma amostra de pacientes aguardando pela cirurgia em centro cirúrgico de hospital público de área metropolitana, o que pode trazer diferenças em comparação à população geral. Segundo, o paciente, por desejabilidade social, pode alterar suas respostas, escondendo ou hipervalorizando seus sintomas com a crença ^{de} acelerar o preparo cirúrgico, fenômeno conhecido como “*impression management*”. E por fim, pacientes com obesidade gravíssima (IMC>50), que devido à dificuldade de locomoção, não participaram, diminuindo a amplitude dos achados. Estas limitações metodológicas foram amenizadas pelo tamanho da amostra, assim como o rigor científico na condução da coleta e análise dos dados que podem possibilitar o expandir dos resultados.

6 - Conclusão

A avaliação dos 393 pacientes candidatos à cirurgia bariátrica, por meio de entrevista semiestruturada, permitiu concluir que:

(1) Os transtornos psiquiátricos foram associados à obesidade grave. Transtornos psiquiátricos foram, além de muito frequentes, persistentes e coocorrentes. Os transtornos de humor foram os quadros mais frequentes, porém, os transtornos de ansiedade foram os mais persistentes e concomitantes com outros transtornos, como uso de substâncias e transtornos alimentares.

(2) Identificou-se três subgrupos com psicopatologias homogêneas na amostra de pacientes candidatos a cirurgia bariátrica: (1) classe de “oligossintomáticos”, (2) classe de “bipolares com comorbidades” e (3) classe de “ansiedade e depressão”. Mulheres e homens com obesidade grave se diferenciaram em relação à frequência dos perfis das classes. Em geral, os homens apresentaram quadros mais graves, agruparam-se com maior frequência na classe “bipolares com comorbidades”, associados com ansiedade, transtornos alimentares e uso de substâncias. Entre as mulheres, predominaram os quadros de ansiedade e depressão.

(3) O índice de massa corporal e a situação trabalhista em homens foram associados com a probabilidade do perfil psicopatológico. Enquanto um maior índice de massa corporal associou-se à chance de pertencer à classe das “bipolares com comorbidades”, estar desempregado associou-se à chance de pertencer à classe “ansiedade/depressão”.

Os transtornos psiquiátricos e a obesidade e a intrincada associação, ainda estão distantes de serem totalmente compreendidos. Os transtornos psiquiátricos em pacientes candidatos à cirurgia bariátrica são persistentes e coocorrentes, e se agrupam de forma singular, com diferentes taxas entre mulheres e homens. A influência das comorbidades no resultado pós-cirúrgico ainda é pouco investigada. No período pré-cirúrgico, a estabilização de sintomas psicopatológicos deve anteceder a indicação para realizar a cirurgia. Casos comórbidos, como uso de substâncias, fase ativa do episódio de humor (depressão ou mania/hipomaníaca), devem ser monitorados pela equipe multidisciplinar. Avaliação contínua de pacientes com obesidade submetidos à cirurgia pela equipe multidisciplinar capacitada é recomendada em todas as fases do processo bariátrico. O

impacto clínico desses perfis de comorbidade deve ser demonstrado em investigações prospectivas. Futuros caminhos sugeridos para investigação são avaliações longitudinais específicas pós-cirúrgicas, que levem o gênero em consideração.

Anexo A - Protocolo da aprovação pelo Comitê de Ética

Hospital das Clínicas da FMUSP
Comissão de Ética para Análise de Projetos de Pesquisa
CAPPesq

Nº Protocolo: 0228/11

Título: "ESPECTRO DO TRANSTORNO BIPOLAR ENTRE PACIENTES OBESOS CANDIDATOS À CIRURGIA BARIÁTRICA"

Pesquisador Responsável: Wang Yuan Pang

Pesquisador Executante: Leorides Severo Duarte Guerra

Finalidade Acadêmica: Mestrado

Departamento: PSIQUIATRIA

A Comissão de Ética para Análise de Projetos de Pesquisa - CAPPesq da Diretoria Clínica do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, **APROVOU / TOMOU CIÊNCIA** na sessão datada de 23/11/2011, do(s) documento(s) abaixo mencionada(s):

- Carta datada de 05/10/2011 - Nova versão do protocolo;
- Cronograma atualizado das atividades realizadas.

A CAPPesq em obediência à Resolução CNS 196/96, solicita ao pesquisador (a) s elaboração de relatório parcial e final.

No caso de relatório parcial é necessário informar o tempo previsto para a conclusão do protocolo e breve resumo dos resultados obtidos.

CAPPesq, 23 de Novembro de 2011

Recebido: 23/11/11, às 12:42
Departamento de Psiquiatria da FMUSP

PROF. DR. EUCLIDES AYRES DE CASTILHO
Coordenador
Comissão de Ética para Análise de
Projetos de Pesquisa - CAPPesq

Anexo B- Protocolo de Anuência Interdepartamental.**PROJETO DE PESQUISA INTERDEPARTAMENTAL****HC-FMUSP**

São Paulo, 07 de maio de 2012.

Ao Departamento de Psiquiatria da FMUSP

O Departamento de Gastroenterologia – Disciplina de Cirurgia do Aparelho Digestivo da Faculdade de Medicina da USP tem ciência da realização do Projeto de Pesquisa, intitulado: "ESPECTRO DO TRANSTORNO BIPOLAR EM PACIENTES OBESOS CANDIDATOS A CIRURGIA BARIÁTRICA", que tem como Unidade responsável originária o Departamento de Psiquiatria da FMUSP.

Cuja respectiva Comissão de Ética é responsável pela sua aprovação bem como o devido encaminhamento para a Cappelq – HCFMUSP e demais comissões necessárias.

São os investigadores responsáveis:

Wang Yuan Pang

Leorides Severo Duarte Guerra

Atenciosamente.

Prof.Dr. Ivan Cecconello

Chefe do Departamento de Gastroenterologia da FMUSP

Anexo C**HOSPITAL DAS CLÍNICAS DA FACULDADE DE MEDICINA DA UNIVERSIDADE DE SÃO PAULO****TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO**

(Instruções para preenchimento no verso)

I - DADOS DE IDENTIFICAÇÃO DO SUJEITO DA PESQUISA OU RESPONSÁVEL LEGAL

1. NOME DO PACIENTE :

DOCUMENTO DE IDENTIDADE Nº :

SEXO : M () F ()

DATA NASCIMENTO:/...../.....

ENDEREÇO

Nº APTO:

BAIRRO:

CIDADE

CEP:.....

TELEFONE: DDD (.....)

1. RESPONSÁVEL LEGAL

NATUREZA (grau de parentesco, tutor, curador etc.)

.....

DOCUMENTO DE IDENTIDADE :.....

SEXO: M () F ()

DATA NASCIMENTO.:/...../.....

ENDEREÇO:

Nº APTO:

BAIRRO:.....

CIDADE:

CEP:

TELEFONE:DDD (.....).....

II - DADOS SOBRE A PESQUISA CIENTÍFICA

1. TÍTULO DO PROTOCOLO DE PESQUISA

- Espectro do Transtorno Bipolar em pacientes candidatos à Cirurgia Bariátrica

2.PESQUISADOR Wang Yuan-Pang

CARGO/FUNÇÃO: Médico da Divisão Médica do Instituto de Psiquiatria do Hospital das Clínicas, FMUSP

INSCRIÇÃO CONSELHO REGIONAL CRM 59946

UNIDADE DO HC-FMUSP: IPQ-HC-FMUSP

3. AVALIAÇÃO DO RISCO DA PESQUISA:

SEM RISCO (x)

RISCO MÍNIMO ()

RISCO MÉDIO ()

RISCO BAIXO ()

RISCO MAIOR ()

(probabilidade de que o indivíduo sofra algum dano como consequência imediata ou tardia do estudo)

4.DURAÇÃO DA PESQUISA:

- Dois anos

III - REGISTRO DAS EXPLICAÇÕES DO PESQUISADOR AO PACIENTE OU SEU REPRESENTANTE LEGAL SOBRE A PESQUISA, CONSIGNANDO:

1- Essas informações estão sendo fornecidas para sua participação voluntária neste estudo, que visa saber quantos pacientes com obesidade grau III apresentam transtornos psiquiátricos.

2- Serão utilizadas entrevistas estruturadas, onde não há necessidade de conhecimentos prévios. Estas entrevistas têm o propósito de diagnosticar possíveis transtornos psiquiátricos.

- 3- Não há nenhum risco ou desconforto na participação dessa pesquisa
- 4- Participando você terá o benefício de receber um diagnóstico preciso de algum transtorno que venha ter e poderá receber eventuais tratamentos
- 5- Em qualquer etapa do estudo, você terá acesso aos profissionais responsáveis pela pesquisa para esclarecimentos de eventuais dúvidas. O principal investigador é o Dr. Wang Yuan-Pang, que pode ser encontrado neste endereço: Núcleo de Epidemiologia Psiquiátrica Instituto de Psiquiatria do Hospital das Clínicas Faculdade de Medicina da Universidade de São Paulo - Rua Dr. Ovídio Pires de Campos, no. 7853o. andar - Ala Norte - Sala 17-CEP 05403-010 - São Paulo - SP – Brasil-Fone/Fax::+55 11 3069-6976. Se você tiver alguma consideração ou dúvida sobre a ética da pesquisa, entre em contato com o Comitê de Ética em Pesquisa (CEP) – Rua Ovídio Pires de Campos, 225 – 5º andar – tel: 3069-6442 ramais 16, 17, 18 ou 20, FAX: 3069-6442 ramal 26 – E-mail: cappesq@hcnet.usp.br
- 6- É garantida a liberdade da retirada de consentimento a qualquer momento e deixar de participar do estudo, sem qualquer prejuízo à continuidade de seu tratamento na Instituição;
- 7- As informações obtidas serão analisadas em conjunto com outros pacientes, não sendo divulgados a identificação de nenhum paciente;
- 8- Você terá direito a ser mantido atualizado sobre os resultados que vierem a ser obtidos
- 9- Não há despesas pessoais para o participante em qualquer fase do estudo, incluindo exames e consultas. Também não há compensação financeira relacionada à sua participação.
- 10- Os dados coletados serão utilizados somente para esta pesquisa;

Acredito ter sido suficientemente informado a respeito das informações que li ou que foram lidas para mim, descrevendo o estudo “Espectro do transtorno bipolar em pacientes obesos candidatos à cirurgia bariátrica”.

Eu discuti com o Dr. Wang Yuan-Pang, sobre a minha decisão em participar nesse estudo. Ficaram claros para mim quais são os propósitos do estudo, os procedimentos a serem realizados, seus desconfortos e riscos, as garantias de confidencialidade e de esclarecimentos permanentes. Ficou claro também que minha participação é isenta de despesas e que tenho garantia do acesso a tratamento hospitalar quando necessário. Concordo voluntariamente em participar deste estudo e poderei retirar o meu consentimento a qualquer momento, antes ou durante o mesmo, sem penalidades ou prejuízo ou perda de

qualquer benefício que eu possa ter adquirido, ou no meu atendimento neste Serviço.

Assinatura do paciente/representante legal Data / /

Assinatura da testemunha Data / /

para casos de pacientes menores de 18 anos, analfabetos, semi-analfabetos ou portadores de deficiência auditiva ou visual.

(Somente para o responsável do projeto)

Declaro que obtive de forma apropriada e voluntária o Consentimento Livre e Esclarecido deste paciente ou representante legal para a participação neste estudo.

Wang Yuan Pang

Assinatura do responsável pelo estudo Data / /

Anexo D

QUESTIONARIO CLÍNICO

I – Identificação

Nome:.....

Idade: (dia/mês/ano). (...../...../.....) Sexo: masculino (....) feminino (....)

Estado Civil: (Se casado, viúvo ou divorciado, há quanto tempo?).....

Quantos filhos:.....

Escolaridade:.....

Profissão:.....

Nacionalidade(Paísde Origem).....

Naturalidade(Cidade de nascimento).....

Endereço residencial.....

.....

Telefone de contato.....

Mora com:(pais, esposo, filhos, sozinhos, outros).....

II- Antecedentes clínicos

Peso(Kg)..... IMC.....

Já apresentou transtornos psiquiátrico/psicológico (Se sim, quais e os tratamentos realizados).....

.....

.....

Alcoolismo (se sim há quanto tempo).....

Uso de droga (se sim há quanto tempo).....

Tentativa de suicídio.....

Histórico de transtornos psiquiátricos/psicológicos na família (Casos diagnosticados/tratamentos/internações).....

.....

Histórico de transtornos alimentares na família (Casos de obesidade, anorexia, bulimia, compulsão alimentar).....

.....

Início da obesidade:.....

Qual foi o maior peso?.....

Comorbidades:.....

Existência de situações traumáticas (sequestros, lutos, acidentes, estupros..).....

Anexo E**ENTREVISTA ESTRUTURADA PARA
TRANSTORNO DO EIXO I DO DSM – IV****Edição para Pacientes****SCID-I/P(Versão 2.0)****CENTRO DE TREINAMENTO DE SCID
NÚCLEO DE EPIDEMIOLOGIA PSIQUIÁTRICA****Instituto de Psiquiatria do Hospital das Clínicas
Faculdade de Medicina da Universidade de São Paulo
R. Dr. Ovídio Pires de Campos, 785-CEP 05403-010, São Paulo-SP-Brasil****Responsável pela tradução e adaptação para o Português**

Prof. Dr. Wang Yuan-Pang

Prof. Dr. Francisco Lotufo Neto

O desenvolvimento do SCID tem apoio parcial de

NIMH Contrato #278-83-0007 (DB) e NIMH Grant # 1 RO1 MH40511

Para citação: First, Michael B., Spitzer, Robert L., Gibbon, Miriam, and Williams, Janet, B.W.

“Structured Clinical Interview for DSM-IV Axis I Disorders-Patient
Edition”(SCID-I/P, Version 2.0 9/98 revision). Biometrics Research Department
New York State Research Institute
722 West 168th. Street
New York, New York 10032

8 – Referências Bibliográficas

1. Abegunde DO, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet*. v. 370, n. 9603, p. 1929-1938. 2007.
2. Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, Rahman A. Global mental health 1 - No health without mental health. *Lancet*. v. 370, n. 9590, p. 859-877. 2007.
3. Schmidt MI, Duncan BD, Silva GA, Menezes AM, Monteiro CA, Barreto SM, Chor D, Menezes PR. Chronic non-communicable diseases in Brazil: burden and current challenges. *Lancet*. v. 377, n. 9781, p. 1949-61, Jun 4. 2011.
4. WHO, W. H. O. Global status report on noncommunicable diseases 2010. Description of the global burden of NCDs, their risk factors and determinants. *World Health Organization*. Geneva, p.176. 2011.
5. Andrade L, Walters EE, Gentil V, Laurenti R. Prevalence of ICD-10 mental disorders in a catchment area in the city of Sao Paulo, Brazil. *Social Psychiatry and Psychiatric Epidemiology*. v. 37, n. 7, p. 316-325. 2002.
6. Bromet, E. Andrade LH, Hwang I, Sampson NA, Alonso J, Girolamo G, Graaf R, Demyttenaere K, Hu C, Iwata N, Karam AN, Kaur J, Kostyuchenko S, Lépine JP, Levinson D, Ronald C Kessler RC. Cross-national epidemiology of DSM-IV major depressive episode. *Bmc Medicine*. v. 9. 2011.
7. Metabólica, S.B.C.B. Mapeamento Obesidade. 2007. Disponível em: <http://www.scb.org.br/pesquisa/pesquisa_sobre_obesidade_no_brasil_2007.zip>. Acesso em: 11/FEB/2014.
8. Simon GE, Von Korff M, Saunders K, Miglioretti DL, Crane PK, van Belle G, Kessler RC. Association between obesity and psychiatric disorders in the US adult population. *Arch Gen Psychiatry*. v. 63, n. 7, p. 824-30. 2006.
9. Scott, KM, McGee MA, Wells JE, Oakley Browne MA. Obesity and mental disorders in the adult general population. *J Psychosom Res*. v. 64, n. 1, p. 97-105. 2008.
10. Rajan TM, Menon V. Psychiatric disorders and obesity: A review of association studies. *J. Postgrad. Med*. 63(3): 182-190. 2017.
11. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCSR). *Arch. Gen. Psychiatry*. 62(6): 617–627. 2005.
12. Andrade LH, Wang YP, Andreoni S, Silveira CM, Alexandrino-Silva C, Siu ER, Nishimura R, Anthony JC, Gattaz WF, Kessler RC, Viana MC. Mental disorders in megacities: finding from the São Paulo megacity mental health survey, *Brazil. PLoS One*. 7(2):e31879. 2012.

13. GBD 2015, Obesity Collaborators. Health effects of overweight and obesity in 195 countries over 25 years. *N. Engl. J. Med.* 377:13-27. 2017.
14. NCD, Risk factor Collaboration (NCD-RisC) 2017. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet.* 390(10113): 2627-2642. 2017.
15. Dawes AJ, Maggard-Gibbons M, Maher AR, Booth MJ, Mlake-Lye I, Beroes JM, Shekelle PG. Mental health conditions among patients seeking and undergoing bariatric surgery: a meta-analysis. *JAMA.* 315(2):150-63. 2016.
16. Duarte-Guerra LS, Coêlho BM, Santo M, Wang YP. Psychiatric Disorders Among Obese Patients Seeking Bariatric Surgery: Results of Structured Clinical Interviews. *Obes Surg.* 25:830-837. 2015.
17. Kalarchian MA, Marcus MD, Levine MD, Courcoulas AP, Pilkonis PA, Ringham RM, Soulakova JN, Weissfeld LA, Rofey DL. Psychiatric disorders among bariatric surgery candidates: relationship to obesity and functional health status. *Am J Psychiatry.* v. 164, n. 2, p. 328-34; quiz 374. 2007.
18. Muhlhans B, Horbach T, De Zwaan M. Psychiatric disorders in bariatric surgery candidates: a review of the literature and results of a German prebariatric surgery sample. *Gen Hosp Psychiatry.* v. 31, n. 5, p. 414-21. 2009.
19. Lin HY, Huang CH, Tai CM, Lin HY, Kao YH, Tsai CC, Hsuan CF, Lee SL, Yen YC. Psychiatric disorders of patients seeking obesity treatment. *BMC Psychiatry.* 13:1. 2013.
20. Malik S, Mitchell JE, Engel S, Crosby R, Wonderlich S. Psychopathology in bariatric surgery candidates: a review of studies using structured diagnostic interviews. *Compr Psychiatry.* 55(2):248-59. 2014.
21. Mauri M, Rucci P, Calderone A, Santini F, Oppo A, Romano A, Rinaldi S, Armani A, Polini M, Pinchera A, Cassano GB. Axis I and II disorders and quality of life in bariatric surgery candidates. *J Clin Psychiatry.* 69(2):295-301. 2008.
22. Apovian CM, Garvey WT, Ryan DH. Challenging Obesity: Patient, Provider, and Expert Perspectives on the Roles of Available and Emerging Nonsurgical Therapies. *Obesity.* 02:S1-S26. 2015.
23. Duarte-Guerra LS, Coêlho BM, Santo MA, Lotufo-Neto F, Wang YP. Morbidity persistence and comorbidity of mood, anxiety, and eating disorders among preoperative bariatric patients. *Psychiatry Res.* 257:1-6. 2017.
24. Mitchell JE, Selzer F, Kalarchian MA, Devlin MJ, Strain GW, Elder KA, Marcus MD, Wonderlich S, Christian NJ, Yanovski SZ. Psychopathology before surgery in the longitudinal assessment of bariatric surgery-3 (LABS-3) psychosocial study. *Surg Obes Relat Dis.* 8(5):533-41. 2012.

25. Desai RA, Manley M, Desai MM, Potenza LM, Gender differences in the association between body mass index and psychopathology. *CNS Spectr.* 14(7):372-83. 2009.
26. Tronieri JS, Wurst CM, Pearl RL, Allisson KC. Sex differences in obesity and mental health. *Curr. Psychiatry Rep.* 19-29. 2017.
27. Observatory, N.O. International Comparisons of Obesity Prevalence. 2011. Disponível em: http://www.noo.org.uk/uploads/doc799_2_International_Comparisons_Obesity_Prevalence2.pdf . Acesso em: 18/FEV/2014.
28. Popkin BM, Adair LS, NG SW. Global nutrition transition and the pandemic of obesity in developing countries. *Nutr Rev.* v. 70, n. 1, p. 3-21. 2012.
29. Oliveira JHA, Yoshida EMP. Avaliação Psicológica de Obesos Grau III Antes e Depois de Cirurgia Bariátrica. São Paulo. *Psicologia: Reflexão e Crítica.* 22: 12-19 p. 2009.
30. Kretschmer E. Körperbau und Charakter. 1931.
31. Spiegel A, Nabel E, Volkow N, Landis S, Li TK. Obesity on the brain. *Nature Neuroscience.* v. 8, n. 5, p. 552-553. 2005.
32. Damaso A. Etiologia da obesidade. Rio de Janeiro: 2003.
33. Sieck G. Obesidade. Porto Alegre, RS: Fundação Faculdade Federal de Ciências Médicas de Porto Alegre. 2009.
34. Monteiro CA, Conde WL, Popkin BM. Income-specific trends in obesity in Brazil: 1975-2003. *American Journal of Public Health.* v. 97, n. 10, p. 1808-1812. 2007.
35. Monteiro CA, Conde WL, Popkin BM. Narrowing socioeconomic inequality in child stunting: the Brazilian experience, 1974-2007. *Bulletin of the World Health Organization.* v. 88, n. 4, p. 305-311. 2010.
36. Monteiro CA, Conde WL, Popkin BM. Is obesity replacing or adding to undernutrition? Evidence from different social classes in Brazil. *Public Health Nutr.* v. 5, n. 1A, p. 105-12. 2002.
37. WHO, World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. Genebra 1995.
38. Ministério Da Saúde. Vigitel Brasil 2006: vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico. Brasília: Ministério da Saúde 2007.
39. Ministério Da Saúde. Vigitel Brasil 2017: vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico. Brasília: Ministério da Saúde 2018.

40. Dobrow IJ, Kamenetz C, Devlin MJ. Aspectos psiquiátricos da obesidade. *Rev Bras Psiquiatria*. 2002-12;24(Supl. v. 3):63-7.
41. Lin EHB, Von Korff M, Consortium WWS. Mental disorders among persons with diabetes-Results from the World Mental Health Surveys. *Journal of Psychosomatic Research*. v. 65, n. 6, p. 571-580. 2008.
42. Ahmed AT, Warton EM, Schaefer CA, Shen L, McIntyre RS. The effect of bariatric surgery on psychiatric course among patients with bipolar disorder. *Bipolar Disorders*. v. 15, n. 7, p. 753-763. 2013.
43. Jimerson DC, Lesem MD, Kaye WH, Hegg AP, Brewerton TD. Eating Disorders And Depression - Is There A Serotonin Connection. *Biological Psychiatry*.v. 28, n. 5, p. 443-454. 1990.
44. Kalarchian MA, Marcus MD, Levine MD, Soulakova JN, Courcoulas AP, Wisinski MS. Relationship of psychiatric disorders to 6-month outcomes after gastric bypass. *Surgery for Obesity and Related Diseases*. v. 4, n. 4, p. 544-549. 2008.
45. Alciati A, D'Ambrosio A, Foschi D, Corsi F, Mellado C, Angst J. Bipolar spectrum disorders in severely obese patients seeking surgical treatment. *J Affect Disord*. v. 101, n. 1-3, p. 131-8. 2007.
46. Rosenberger PH, Henderson KE, Grilo CM. Psychiatric disorder comorbidity and association with eating disorders in bariatric surgery patients: A cross-sectional study using structured interview-based diagnosis. *J Clin Psychiatry*. v. 67, n. 7, p. 1080-5. 2006.
47. Sarwer DB, Fabricatore AN. Psychiatric considerations of the massive weight loss patient. *Clinics in Plastic Surgery*. v. 35, n. 1, p. 1. 2008.
48. Calkin C, van de Velde C, Růzicková M, Slaney C, Garnham J, Hajek T, O'Donovan C, Alda M. Can body mass index help predict outcome in patients with bipolar disorder? *Bipolar Disorders*. v. 11, n. 6, p. 650-656. 2009.
49. Vannucchi G, Toni C, Maremmanni I, Perugi G. Does obesity predict bipolarity in major depressive patients? *Journal of Affective Disorders*. v. 155, p. 118-122. 2014.
50. Diniz M, Sander M, Almeida S. Critérios de Eficácia do Tratamento Cirúrgico e Avaliação da Qualidade de Vida. São Paulo: Atheneu. 2002.
51. Garrido AJ. Cirurgia da obesidade como estamos. *Revista Abeso*. 2 (4) 2001.
52. Sjöström L, Narbro K, Sjöström CD, Karason K, Larsson B, Wedel H, Lystig T, Sullivan M, Bouchard C, Carlsson B, Bengtsson C, Dahlgren S, Gummesson A, Jacobson P, Karlsson J, Lindroos AK, Lönroth H, Näslund I, Olbers T, Stenlöf K, Torgerson J, Agren G, Carlsson LM; Swedish Obese

- Subjects Study. Effects of bariatric surgery on mortality in Swedish obese subjects. *New England Journal of Medicine*. v. 357, n. 8, p. 741-752. 2007.
53. Picot J, Jones J, Colquitt JL, Gospodarevskaya E, Loveman E, Baxter L, Clegg AJ. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. *Health Technology Assessment*. v. 13, n. 41, p. 1. 2009.
 54. Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, Rosamond WD, Lamonte MJ, Stroup AM, Hunt SC. Long-term mortality after gastric bypass surgery. *New England Journal of Medicine*. v. 357, n. 8, p. 753-761. 2007.
 55. Schwartz A, Etchechoury L, Collet D. Outcome after laparoscopic gastric bypass for super-super obese patients. *Journal of Visceral Surgery*. v. 150, n. 2, p. 145-149. 2013.
 56. Mateo Gavira MI, Vílchez López FJ, Cayón Blanco M, García Valero A, Escobar Jiménez L, Mayo Ossorio MA, Pacheco García JM, Vázquez Gallego JM, Aguilar Diosdado M. Effect Of Gastric Bypass On The Cardiovascular Risk And Quality Of Life In Morbid Obese Patients. *Nutricion Hospitalaria*. v. 29, n. 3, p. 508-512. 2014.
 57. Fandiño J, Benchimol AK, Coutinho WF, Appolinario JC. Cirurgia bariátrica: aspectos clínicos-cirúrgicos e psiquiátricos. *Revista Psiquiatria do Rio Grande do Sul*. 26(1): 47-51 2004.
 58. Appolinario J, Claudino A. Transtornos alimentares. *Revista Brasileira de Psiquiatria*. 22: 28-31 p. 2002.
 59. Guisado M, Leal V. Psychopathological differences between morbidly obese compulsão alimentar eaters and non-compulsão alimentar eaters after bariatric surgery. *Eating Weight Disorders*. 8(4):315-8. 2003.
 60. Baskaran A, Cha DS, Powell AM, Jalil D, McIntyre RS. Sex differences in rates of obesity in bipolar disorder: postulated mechanisms. *Bipolar Disorders*. v. 16, n. 1, p. 83-92. 2014.
 61. Gordon PC, Kaio GH, Sallet PC. Aspects of psychiatric care for obese patients under bariatric treatment: a review. *Revista De Psiquiatria Clinica*. v. 38, n. 4, p. 148-154. 2011.
 62. Matos M, Zanella M. Alterações do comportamento alimentar, ansiedade, depressão e imagem corporal em pacientes como obesidade classe III. *Revista ABESO*. Ano 3(9) 2002.
 63. Magdaleno RJr, Chaim EA, Turato ER. Understanding the Life Experiences of Brazilian Women after Bariatric Surgery: a Qualitative Study. *Obesity Surgery*. v. 20, n. 8, p.1086-1089. 2010.

64. Schinnar, AP, Rothbard AB, Kanter R, Jung YS. An empirical literature review of definition of severe and persistent mental illness. *Am. J. Psychiatry*. 147 (12),1602–1608. 1990.
65. Ruggeri M, Leese M, Thornicroft G, Bisoffi G, Tansella M. Definition and prevalence of severe and persistent mental illness. *Br. J. Psychiatry*. 177 (2), 149–155. 2000.
66. Yen YC, Huang CK, Taic CM. Psychiatric aspects of bariatric surgery. *Curr. Opin. Psychiatry*. 27 (5), 374–379. 2014.
67. Fuchs C, Steinberg DM, Poyurovsky M. On the estimation and comparison of lifetime morbid risks. *Journal of Data Science*; 8(4):645–664. 2010.
68. Kessler RC, Avenevoli S, Costello EJ, Georgiades K, Green JG, Gruber MJ, He JP, Koretz D, McLaughlin KA, Petukhova M, Sampson NA, Zaslavsky AM, Merikangas KR. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the national comorbidity survey replication adolescent supplement. *Arch. Gen. Psychiatry* 69 (4), 372–380. 2012.
69. Pickering RP, Grant BF, Chou SP, Compton WM. Are overweight, obesity, and extreme obesity associated with psychopathology? Results from the national epidemiologic survey on alcohol and related conditions. *J. Clin. Psychiatry* 68, 998–1009. 2007.
70. Pataky Z, Carrad I, Golay A. Psychological factors and weight loss in bariatric surgery. *Curr. Opin. Gastroenterol*. 27 (2), 167–173. 2011.
71. Schellevis FG, van der Velden J, van de Lisdonk E, van Lijk JT, van Weel C. Comorbidity of chronic disease in general practice. *J Clin Epidemiol*. 46(5):469-73. 1993.
72. Barry D, Pietrzak RH, Petry NM. Gender differences in associations between body mass index and DSM-IV mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Ann. Epidemiol*. 18, 458–466. 2008.
73. Mitchell JE, King WC, Pories W, Wolfe B, Flum DR, Spaniolas K, Bessler M, Devlin M, Marcus MD, Kalarchian M, Engel S, Khandelwal S, Yanovski S. Binge eating disorder and medical comorbidities in bariatric surgery candidates. *Int J Eat Disord*. 48(5):471-6. 2015.
74. Barry D, Petry NM. Associations between body mass index and substance use disorders differ by gender: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Addict. Behav*. 34, 51–60. 2009.

75. Neuman RJ, Heath A, Reich W, Bucholz KK, Madden PAF, Sun L, Todd RD, Hudziak JJ. Latent class analysis of ADHD and comorbid symptoms in a population sample of adolescent female twins. *J Child Psychol Psychiatry*. v. 42, n. 7, p. 933-42. 2001.
76. Clogg CC. The impact of sociological methodology on statistical methodology. *Statist. Sci.* V. 7. Number 2, 183-196. 1992.
77. Lazarsfeld P, Henry N. Latente structure analyses. Boston: Houghton-Mifflin, 1968.
78. Goodman LA. A latent class analysis: the empirical study of latent types, latent variables and latent structures. Separata de: Hagenaars CA, Mccutcheon AL. Applied latent class analysis. *Cambridge University*. p. 3-55. 2002.
79. Sullivan PF, Kessler RC, Kendler KS. Latent class analysis of lifetime depressive symptoms in the national comorbidity survey. *AM J Psychiatry*. 155:1398-1406. 1998.
80. Dubois B, Czellar S, Laurent G. Consumer segments based on attitudes toward luxury: empirical evidence from twenty countries. *Marketing letters*. Netherlands, v. 16, n. 2, p. 115-128. 2005.
81. Swanson SA, Horton NJ, Crosby RD, Micali N, Sonnevile KR, Eddy K, Field AE. A latent class analysis to empirically describe eating disorders through developmental stages. *Int. J. Eat. Disord.* 47, 762–772. 2014.
82. Wade TD, Crosby RD, Martin NG. Use of latent profile analysis to identify eating disorders phenotypes in an adult Australian twin cohort. *Arch. Gen. Psychiatry*. 63, 1377–1384. 2006.
83. Schafer L, Hubner C, Carus C, Herbing B, Seyfried F, Kaiser S, Schutz T, Dietrich A, Hilbert A. Identifying prebariatric subtypes based on temperament traits, emotion dysregulation, and disinhibited eating: a latent profile analysis. *Int. J. Eat. Disord.* 50, 1172–1182. 2017.
84. Sysko R, Zakarin EB, Devlin MJ, Bush J, Walsh BT. A latent class analysis of psychiatric symptoms among 125 Adolescents in a bariatric surgery program. *Int. J. Pediatr. Obes.* 6, 289–297. 2011.
85. Martínez EP, González ST, Vicente MM, van der Hofstadt Roman CJ, Rodriguez-Marin J. Psychopathology in a sample of candidate patients for bariatric surgery. *Int. J. Psychiatry Clin. Pract.* 17, 197–205. 2013.
86. Alexandrino-Silva C, Wang YP, Viana MC, Bulhões RS, Martins SS, Andrade LH. Gender differences insymptomatic profiles of depression: results from the São Paulo Megacity Mental Health Survey. *J. Affect. Disord.* 147, 355–364. 2013.

87. Kessler RC, McGonagle KA, Nelson CB, Hughes M, Swartz M, Blazer DG. Sex and depression in the National Comorbidity Survey II: cohort effects. *J. Affect. Disord.* 30, 15–26. 1994.
88. Lwanga SK, Lemeshow S. Sample size determination in health studies: a practical manual. Geneva: World Health Organization. 1991.
89. Lee L, D EEE. Calculadora Eletrônica. 2010. Disponível em: <http://www.lee.dante.br>.
90. First MB, Spitzer RL, Gibbon ML, Williams JBW. Structured Clinical Interview for DSM-IV- TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P). New York: Biometrics Research: New York State Psychiatric Institute. 2002.
91. Hartmann AS, Mark J, Gorman MJ, Sogg E, Lamont EM, Eddy KT, Anne E. Becker AE, Thomas JJ. Screening for DSM-5 Other Specified Feeding or Eating Disorder in a Weight-Loss Treatment–Seeking Obese Sample. *Prim Care Companion CNS Disord.* 16(5). 2004.
92. Green BF. Latent structure analysis and its relation to factor analysis. *Journal of the American Statistical Association.* 47: 71-76. 1952.
93. Habberman SJ. The analysis of residuals in cross-classified tables. *Biometrics* 29: 205-220. 1973.
94. Agresti A. Categorical Data Analysis. Second Edition. Wiley Series in Probability and Statistics. 2002.
95. Vuong Q. Likelihood ratio tests for model selection and non-nested hypotheses. *Econometrica.* 57, 307–333. 1989.
96. Lo Y, Mendell N, Rubin D. Testing the number of components in a normal mixture. *Biometrika.* 88, 767–778. 2001.
97. Wu Q. Class extraction and classification accuracy in latent class models. Unpublished doctoral dissertation, Pennsylvania State University. 2009.
98. Carragher N, Adamson G, Butting B, McCann S. Subtypes of depression in a nationally representative sample. *Journal of Affective Disorders.* 113: 88-99. 2009.
99. Nylund K, Asparouhov T, Muthén, BO. Deciding the number of classes in latent class analysis and growth mixture modelling: a Monte Carlo simulation study. *Structural Equation Modeling.* 14: 535-569. 2007.
100. Muthén L, Muthén, B. Mplus User's Guide. Muthén&Muthén, Los Angeles, CA. 1998– 2010.

101. Ohayon MM, Schatzberg AF. Using chronic pain to predict depressive morbidity in the general population. *Arch Gen Psychiatry*. 60:39–47. 2003
102. de Zwaan M, Enderle J, Wagner S, Muhlhans B, Ditzen B, Gefeller O, Mitchell JE, Müller A. Anxiety and depression in bariatric surgery patients: a prospective, follow-up study using structured clinical interviews. *J Affect Dis*. 2011 Sep;133(1-2):61-8.
103. Gariepy G, Nitka D, Schmitz N. The association between obesity and anxiety disorders in the population: a systematic review and meta-analysis. *International Journal of Obesity*. 34, 407–419. 2010.
104. McElroy SL, Keck PE Jr. Metabolic syndrome in bipolar disorders: a review with a focus on bipolar depression. *J Clin Psychiatry*. Jan; 75(1): 46-61. 2014.
105. Batic-Mujanovic O, Poric S, Pranjic N, Ramic E, Alibasic E, Karic E. Influence of unemployment on mental health of the working age population. *Mater Sociomed*. 29(2):92-96. 2017.
106. Kochkodan J, Telem DA, Ghaferi AA. Physiologic and psychological gender differences in bariatric surgery. *Surg Endosc*. 32(3):1382-1388. 2018.
107. Bond DJ, E Silveira E, MacMillan EL, Torres IJ, Lang DJ, W Su W, Honer WG, Lam RW, Yatham LN. Diagnosis and body mass index effects on hippocampal volumes and neurochemistry in bipolar disorder. *Transl Psychiatry*. 7(3): e1071. 2017.
108. Eichen DM, Matheson BE, Appleton-Knapp SL, Boutelle KN. Neurocognitive Treatments for Eating Disorders and Obesity. *Curr Psychiatry Rep*. 19(9):62. 2017.

9 - Apêndice

Produção Científica:

- A. **Duarte-Guerra LS**, Coêlho BM, Santo MA, Wang, YP. Psychiatric disorders among obese patients seeking bariatric surgery: results of structured clinical interviews. *Obes Surg* 25:830-837. 2015.
- B. **Duarte-Guerra LS**, Gorenstein C, Paiva-Medeiros PF, Santo MA, Lotufo Neto F, Wang YP. Clinical utility of the Montgomery-Åsberg Depression Rating Scale for the detection of depression among bariatric surgery candidates. *BMC Psychiatry*. 2016 Apr 30;16:119. doi: 10.1186/s12888-016-0823-8.
- C. Paiva-Medeiros PF, **Duarte-Guerra LS**, Santo MA, Lotufo-Neto F, Wang YP. Psychometric Properties of the Montgomery-Åsberg Depression Rating Scale in Severely Obese Patients. *Span J Psychol*. 2015 Sep 14;18:E69. doi: 10.1017/sjp.2015.072.
- D. Lasagni V, Palma R, Rios B, Vázquez-Velásques V, **Duarte-Guerra LS**, Malischesqui Paegle I, Graf B, Lyng V, Sánchez Salvatierra M. Propuesta de guía para el tratamiento de la reganancia de peso después de cirugía bariátrica. Proposal of a guide for the treatment of weight regain after bariatric surgery. *Bariátrica & Metabólica Ibero-Americana*. 8.2.12:2318-2322. 2018.
- E. Coêlho BM, Santana GL, **Duarte-Guerra LS**, Viana MC, Lotufo-Neto, Andrade LH, Wang YP. The role of gender in the structure of networks of childhood adversity. *Psychiatry Research*. 2018. doi: <https://doi.org/10.1016/j.psychres.2018.09.059>.

A. **Duarte-Guerra** LS, Coêlho BM, Santo MA, Wang, YP. Psychiatric disorders among obese patients seeking bariatric surgery: results of structured clinical interviews. *Obes Surg* 25:830-837. 2015.

Reprinted by permission from Springer Nature
and Copyright Clearance Center; Obesity Surgery.
License Number 4405380935782.

Psychiatric Disorders Among Obese Patients Seeking Bariatric Surgery: Results of Structured Clinical Interviews

Leorides Severo Duarte-Guerra · Bruno Mendonça Coêlho ·
Marco Aurélio Santo · Yuan-Pang Wang

Published online: 31 October 2014
© Springer Science+Business Media New York 2014

Abstract

Background Obesity and psychiatric disorders are burdensome health problems commonly observed in general population and clinical samples. However, non-standardized assessment and small size of the sample might hamper conclusions of the investigations. The objective of this study is to replicate previous findings on frequency of psychiatric disorders and associated factors among obese patients seeking bariatric surgery, assessed through standardized interview.

Material and Method The sample was comprised of 393 treatment-seeking obese patients (79.1 % women; mean age 43.0 years, mean BMI 47.8 kg/m²) recruited from a university-based bariatric center. Trained clinicians ascertained the psychiatric diagnosis of the participants through structured clinical interview for DSM-IV Axis I diagnosis (SCID-I).

Results The current rate of any psychiatric disorders was 57.8 % (58.5 % men vs. 57.6 % women). The current anxiety disorders were the most frequent diagnosis (46.3 %) among those participants with current disorder. Age and educational level were associated with the likelihood of presenting current psychiatric disorders. The lifetime rate of any psychiatric disorders was 80.9 % (81.7 men vs. 80.7% women). Lifetime affective disorders were the most frequent diagnosis (total 64.9%; bipolar disorders 35.6% and depressive disorders 29.3%). About half of the sample presented 3 or more

concurrent disorders among those respondents presenting any lifetime psychiatric disorders.

Conclusions Psychiatric disorders are frequent conditions among obese patients before bariatric surgery. Systematic assessment of patients in the pre-surgical phase is recommended. Prognostic implications of psychiatric disorders on surgery outcome should be demonstrated in follow-up study.

Keywords Psychiatric disorders · Standardized interview · Obesity · Bariatric surgery

Introduction

According to the World Health Organization projections, noncommunicable diseases (NCD) are responsible for the major burden of diseases on the globe, where several conditions are mediated by metabolic factors [1]. Among the NCD, obesity and psychiatric disorders emerge as health challenges for the next decades [2–4]; these two conditions are priorities in the public health agenda [5–8], due to their disabling effects on the individuals' quality of life, reduced labor ability, higher use of health services, and societal costs [7, 9, 10].

The tendency of overweight/obesity seems to be associated with the level of country development, suggesting an over-nourishment dietary pattern in the population residing in more industrialized societies [11]. However, since the 1990s, the tendency of obesity became an impending global pandemic, also in low- and middle-income populations, being associated with diabetes, hypertension, and cardiovascular diseases [1]. High calorie food intake, sedentary lifestyle habits, and urban living are risk factors that shorten the life expectancy due to cardiovascular morbidities. Also, psychiatric disorders seem to cluster together with obesity, and both disorders make-up a complex interplay between dietary intake, environmental exposure, and genetic risk. High rates of psychiatric disorders

Parts of this investigation were presented during the 18th World Congress of International Federation for the Surgery of Obesity & Metabolic Disorders, Istanbul, Turkey (28–31 August, 2013).

L. S. Duarte-Guerra · B. M. Coêlho · Y.-P. Wang (✉)
Department & Institute of Psychiatry, University of São Paulo
Medical School, Rua Dr. Ovídio Pires de Campos, no. 785,
05403-010 São Paulo, SP, Brazil
e-mail: gnep_inbox@hotmail.com

M. A. Santo
Department of Surgery, University of São Paulo Medical School, Av.
Enéas de Carvalho Aguiar, no. 255, 05403-900 São Paulo, SP, Brazil

among obese population might suggest mutual causal relationships or shared common etiological factors [12, 13].

Little information regarding harmful obesity in non-developed countries is available, and most existing studies were conducted in developed countries [9, 14–18]. More than 35 % of the world's population is overweight [19]; while 7 % of the lower/middle-income countries population is considered obese, the rate reaches over three times higher in upper-income countries. For instance, Latin America [20] and Asia [21] are regions passing through both epidemiological and nutritional transition, where the health burden of infectious diseases is gradually replaced by NCD and malnutrition by obesity [11, 22, 23]. Paradoxically, in rapidly advancing economy, countries like Brazil, about 30 million of obese people live jointly with undernourished people. The figures of obesity/overweight represent 18 % of Brazilian population [19], being 3 % classified as morbid obesity [24]. Accordingly, the bariatric interventions emerged as life-saving resource for class III obese, which respond poorly to noninvasive treatments [10, 25, 26]. Likewise the worldwide growth of gastroplastic surgeries [13, 26], this intervention is rapidly popularized in Brazil. From 2001 to 2008, the number of bariatric procedures increased by 542 % in Brazilian health system, at an annual expenditure of over 15 million real [27].

Nevertheless, reliable knowledge on pre-surgical patients in middle-income countries represents a serious gap. The majority of studies on psychiatric morbidities in surgical obesity were conducted in regions with established economy, such as the USA [18, 28–31] and Europe [32–34], with some investigations conducted with limited sample size [29, 31–33]. The existing studies in non-developed countries such as Brazil have not used reliable interview to assess psychiatric disorders [35, 36], which may hamper the data comparability.

The aim of this study is to estimate the current and lifetime frequency of psychiatric disorder among a sizable sample of patients seeking bariatric surgery. After assessing psychiatric disorders through a standardized interview (SCID-I), the associated factors of psychiatric disorders were determined.

Methods

This is a cross-sectional study for assessing psychiatric disorders among treatment-seeking obese patients.

Participants

The participants were recruited from the largest Brazilian university-based bariatric center, where more than 200 surgeries were completed per year, without expenses for the patients. The multi-disciplinary team is comprised of surgeon, psychologist, nurse, and dietician. The technique of Roux-en-Y gastric bypass is the preferred surgical procedure.

To enter in the program, participants should meet the criterion of obesity class III ($\text{BMI} \geq 40 \text{ kg/m}^2$), aged ≥ 18 years, and able to understand the risks and benefits of surgery. Thereafter, they were ranked in an ordered waiting list and preoperative workup was performed. Along the year of 2010, over 500 patients were enrolled in the program. Previous severe psychiatric disorders (e.g., psychosis, intellectual disability), as detected during psychological assessment, were conditions that preclude bariatric surgery. Language difficulties, mobility/geographic problems (e.g., due to excessive weight and/or dwelling in distant places), and previous bypass surgery are additional exclusion criteria.

The first contact was made by telephone, and the patients were invited to participate in the study after brief explanation. From the first 500 eligible patients in the list, 63 individuals declined to participate during the telephone contact and 44 were excluded from the clinical interview due to severe psychiatric illness (1 psychotic and 1 intellectual disability), previous bariatric surgery (5), and mobility difficulty (37). The final sample was comprised of 393 individuals (participation rate 78.6 %).

Table 1 shows the demographic characteristics of the sample, comprising 79.1 % women, with mean age of 43.0 years (standard deviation [SD] 11.5). The majority was married/cohabiting (51.1 %), and one-quarter were single. The mean years of education were 9.6 (SD 3.6). The mean BMI was 47.8 kg/m^2 (SD 7.5; range 31.2–92.1), being men significantly more obese than women ($\text{BMI } 50.2 \text{ vs. } 46.4$; $p=0.01$). The BMI correlated significantly with age ($p<0.0001$) (see Table 2).

Instruments

The structured clinical interview for **DSM-IV** Axis I disorder (SCID-I) [37] is a standardized semi-structured interview

Table 1 Sociodemographic characteristics of bariatric surgery candidates ($n=393$)

Variable	N	(%)
Sex		
Female	311	(79.1)
Male	82	(20.9)
Marital status		
Married	201	(51.1)
Single	100	(25.4)
Separated/divorced	65	(16.5)
Widowed	26	(6.6)
Education		
1–8 years	138	(35.1)
9–12 years	175	(44.5)
>12 years	80	(20.4)

Table 2 Frequency of current SCID-I psychiatric disorders in bariatric surgery candidates ($n=393$)

Psychiatric disorder	Total (<i>N</i> =393) <i>n</i> (%)	Women (<i>N</i> =311) <i>n</i> (%)	Men (<i>N</i> =82) <i>n</i> (%)	<i>p</i>	
Any psychiatric disorder	227 (57.8)	179 (57.6)	48 (58.5)	0.87	
Any affective disorder	85 (21.6)	68 (21.9)	17 (20.7)	0.83	
Any bipolar disorder	54 (13.7)	41 (13.2)	13 (15.9)	0.53	
Bipolar disorder I	8 (2.0)	6 (1.9)	2 (2.4)	0.67	
Bipolar disorder II	29 (7.4)	21 (6.8)	8 (9.8)	0.51	
Bipolar disorder NOS	17 (4.3)	14 (4.5)	3 (3.7)	1.00	
Any depressive disorder	31 (7.9)	27 (8.7)	4 (4.9)	0.36	
Major depression	27 (6.9)	23 (7.4)	4 (4.9)	0.62	
Dysthymia	4 (1.0)	4 (1.3)	—	—	
Any anxiety disorder	182 (46.3)	147 (47.3)	35 (42.7)	0.65	
Panic disorder	9 (2.3)	8 (2.6)	1 (1.2)	0.69	
Agoraphobia	22 (5.6)	21 (6.8)	1 (1.2)	0.06	
Social phobia	36 (9.2)	28 (9.0)	8 (9.8)	0.90	
Specific phobia	67 (17.0)	55 (17.7)	12 (14.6)	0.45	
PTSD	10 (2.5)	8 (2.6)	2 (2.4)	1.00	
Obsessive-compulsive	14 (3.6)	13 (4.2)	1 (1.2)	0.32	
Generalized anxiety	94 (23.9)	79 (25.4)	15 (18.3)	0.11	
Anxiety NOS	21 (5.3)	17 (5.5)	4 (4.9)	1.00	
Any substance use disorder	12 (3.1)	6 (1.9)	6 (7.3)	0.01	
Alcohol use disorder	12 (3.1)	6 (1.9)	6 (7.3)	0.01	
Drug use disorder	2 (0.5)	1 (0.3)	1 (1.2)	0.37	
Any eating disorder	79 (20.1)	62 (19.9)	17 (20.7)	0.87	
Binge eating disorder	65 (16.5)	48 (15.4)	17 (20.7)	0.65	
Bulimia nervosa	14 (3.6)	14 (4.5)	—	—	
Any disorder (<i>N</i> , %)	227 (57.8)	179 (57.6)	48 (58.5)	0.87	
No disorder	166 (42.2)	132 (42.4)	34 (41.5)		
1 disorder	105 (26.7)	80 (25.7)	25 (30.5)		
2 disorders	61 (15.5)	48 (15.4)	13 (15.9)		
3+ disorders	61 (15.5)	51 (16.4)	10 (12.2)	0.73	
GAF (mean, SD)	76.8 (12.3)	77.3 (11.7)	74.6 (14.4)	<i>t</i> =0.155	−0.07
BMI, kg/m ² (mean, SD)	47.8 (7.5)	46.4 (6.6)	50.2 (9.6)	<i>t</i> =−3.406	0.01
Age, year (mean, SD)	43.0 (11.5)	43.9 (11.4)	42.7 (12.0)	<i>t</i> =0.269	0.79

Cells with less than five were used Fisher's statistics for p value

NOS not otherwise specified, PTSD post-traumatic stress disorder, GAF global assessment functioning, BMI body mass index

widely accepted as the gold standard to make diagnosis of psychiatric disorders listed in DSM-IV [38]. After screening for the presence of core psychopathology, the interviewer should investigate if the respondents meet the criteria for affective disorders (section A, D), psychotic disorders (C, D), substance use disorders (SUD) (E), anxiety disorders (F), somatoform disorders (G), eating disorder (H), and adjustment disorders (I). The diagnostic strategy adopted by SCID-I is top-down, i.e., the presence of symptoms should be checked for the criteria for the suspected psychiatric diagnosis. Considerable evidence of reliability and validity was reported in several patient samples [39].

We used the patient version of SCID-I, which allow recording disorders for both current and lifetime period. The sections of psychotic disorders and somatoform disorders were omitted to shorten the time of application. Additionally, psychotic patients are routinely excluded as candidate for bariatric surgery. Before finishing the interview, the interviewer also scored the global assessment functioning (GAF) of the patients, as their best role functioning in the past year [40, 41].

Six clinical psychologists with previous experience in obesity and bariatric surgery were trained in a 3-day standard course of SCID-I, followed by a 60-h calibration practice. Arbitrary pairs of researchers assessed the first 15 patients in

Table 3 Frequency of lifetime SCID-I psychiatric disorders in bariatric surgery candidates ($n=393$)

Psychiatric disorder	Total ($N=393$) n (%)	Women ($N=311$) n (%)	Men ($N=82$) n (%)	p
Any psychiatric disorder	318 (80.9)	251 (80.7)	67 (81.7)	0.84
Any affective disorder	255 (64.9)	200 (64.3)	55 (67.1)	0.64
Any bipolar disorder	140 (35.6)	103 (33.1)	37 (45.1)	0.04
Bipolar disorder I	20 (5.1)	13 (4.2)	7 (8.5)	0.11
Bipolar disorder II	55 (14)	42 (13.5)	13 (15.9)	0.59
Bipolar disorder NOS	65 (16.5)	48 (15.4)	17 (20.7)	0.25
Any depressive disorder	115 (29.3)	97 (31.2)	18 (22.0)	0.10
Major depressive disorder	108 (27.5)	90 (28.9)	18 (22.0)	0.21
Minor depressive disorder	2 (0.5)	2 (0.6)	–	–
Dysthymia	5 (1.3)	5 (1.6)	–	–
Any anxiety disorder	215 (54.7)	177 (56.9)	38 (46.3)	0.09
Panic disorder	35 (8.9)	29 (9.3)	6 (7.3)	0.57
Agoraphobia	42 (10.7)	41 (13.2)	1 (1.2)	0.001
Social phobia	50 (12.7)	41 (13.2)	9 (11.0)	0.59
Specific phobia	92 (23.4)	77 (24.8)	15 (18.3)	0.22
PTSD	12 (3.1)	8 (2.6)	4 (4.9)	0.28
Obsessive-compulsive	25 (6.4)	22 (7.1)	3 (3.7)	0.32
Anxiety NOS	21 (5.3)	17 (5.5)	4 (4.9)	1.00
Any substance use disorder	69 (17.6)	39 (12.5)	30 (36.6)	<0.0001
Alcohol use disorder	57 (14.5)	30 (9.6)	27 (32.9)	<0.0001
Drug use disorder	27 (6.9)	17 (5.5)	10 (12.2)	0.03
Any eating disorder	138 (35.1)	109 (35.0)	29 (35.4)	0.96
Binge eating disorder	117 (29.8)	89 (28.6)	28 (34.1)	0.33
Bulimia nervosa	36 (9.2)	34 (10.9)	2 (2.4)	0.02
Any disorder (N , %)	318 (80.9)	251 (80.7)	67 (81.7)	0.84
No disorder	75 (19.1)	60 (19.3)	15 (18.3)	
1 disorder	76 (19.3)	59 (19.0)	17 (20.7)	
2 disorders	88 (22.4)	70 (22.5)	18 (22.0)	
3+ disorders	154 (39.2)	122 (39.2)	32 (39.0)	0.99

Cells with less than five were used Fisher's statistics for p value

NOS not otherwise specified, PTSD post-traumatic stress disorder, OCD obsessive-compulsive disorder

order to estimate the between-rater agreement. The kappa coefficient [42] for lifetime psychiatric disorders was $k=0.81$. Thereafter, from November 2010 to March 2012, eligible patients were consecutively and randomly assigned to be face-to-face assessed [42]. The average duration of interview ranged between 60 to 90 min [37].

The ethics committee of the University of São Paulo Medical School approved the study. Participants were assured that information provided for research would not influence their eligibility for surgery. All participants have signed an informed consent.

Statistical Analysis

Descriptive analysis calculated the demographic variable and prevalence of current and lifetime DSM-IV Axis I disorders. Chi-square test and t test compared differences for categorical

variables and continuous variable, respectively. Two models of multivariate logistic regression determined the likelihood of factors associated to axis I psychopathology. The dependent variables were current and lifetime psychiatric disorders and independent variables were sex (men, women), marital status (married/cohabiting, separated, widowed, and never married), occupation (employed, unemployed), BMI (kg/m^2), age (years), and education (years). All analyses were performed with SPSS 21.0/PASW [43]. The level of statistical significance was 0.05, for two-tailed tests.

Results

For the total sample, 57.8 % of the subjects presented any disorders at the moment of the interview (Table 2). The

Table 4 Associated factors of psychiatric disorders among treatment-seeking obese patients with any current, and any lifetime disorders ($n=393$)

Variable		Any current disorders OR (95% CI)	Any lifetime disorders OR (95% CI)
Gender	Women	1.00	1.00
	Men	0.89 (0.52–1.50) Wald $\chi^2=0.20$	0.93 (0.48–1.79) Wald $\chi^2=0.05$
Age (years)		0.97 (0.95–0.99) Wald $\chi^2=7.71^*$	0.99 (0.96–1.01) Wald $\chi^2=1.15$
Marital status	Married/cohabiting	1.00	1.00
	Separated	0.90 (0.53–1.52)	0.86 (0.44–1.69)
	Widowed	1.80 (0.66–4.87)	0.98 (0.29–3.30)
	Never married	0.71 (0.37–1.43) Wald $\chi^2=3.54$	0.65 (0.28–1.47) Wald $\chi^2=1.28$
Education (years)		0.92 (0.86–0.98) Wald $\chi^2=7.00^*$	0.93 (0.86–1.01) Wald $\chi^2=2.82$
BMI (kg/m^2)		0.99 (0.96–1.02) Wald $\chi^2=0.50$	0.99 (0.96–1.03) Wald $\chi^2=0.12$
Occupations	Employed	1.00	1.00
	Unemployed	0.90 (0.58–1.40) Wald $\chi^2=0.22$	0.90 (0.52–1.55) Wald $\chi^2=0.16$
Hosmer and Lemeshow test		$\chi^2=3.14, p=0.93$	$\chi^2=11.84, p=0.16$

BMI body mass index

* $p<0.05$

frequency of any current psychiatric disorder was 58.5 and 57.6%, respectively, for men and women. Anxiety disorders were the most common class (46.3 %), and generalized anxiety disorder (GAD) was the most frequent disorder (23.9 %), followed by phobias. The second most frequent class of disorders were affective disorders (21.6 %), bipolar disorders II (7.4 %) and major depressive disorder (6.9 %) being the most common disorders in this class. The frequency of eating disorders was 20.1 %, with binge eating disorder being 16.5 %. A total of 3.1 % of the sample reported any SUD, with men being significantly more likely than women to meet the criteria for such disorders ($p=0.01$). The mean GAF score was 77.0 (SD 12.0, range 40–98). Among those patients diagnosed with any current disorders, 26.7 % presented one disorder, 15.5 % two disorders, and 15.5 % three or more disorders concurrently.

Table 3 shows lifetime rates of psychiatric disorders for the total sample and by gender. Overall, 80.9 % of the participants reported at least one lifetime psychiatric diagnosis. There was no gender difference (81.7 % men and 80.7 % women). Affective disorders were the most frequent category of lifetime disorders (64.9 %). Bipolar disorders were the most common disorders (35.6 %), and 16.5 % of the patients presented bipolar disorder not otherwise specified. Depressive disorders were the second most frequent group of lifetime disorders (29.3 %), with major depressive disorder being the most

common (27.5%). Men were significantly more likely than women ($p=0.04$) to meet the criteria for lifetime bipolar disorders. Lifetime anxiety disorders were present in 54.7 % of participants. Eating disorders were diagnosed in 35.1 %, with binge eating disorder being 29.8 %. Women were significantly more likely than men to meet the criteria for lifetime for bulimia ($p=0.02$). A total of 17.6 % of patients reported any SUD, and men were significantly more likely than women to present a SUD such as alcohol (respectively, 32.9 and 9.6 %) and drugs (12.2 and 5.5 %). Among those with any psychiatric disorder, about 19 % presented one single disorder, 22 % two, and 39 % three or more comorbid disorders. Altogether, psychiatric disorders are considerably stable across lifespan, with anxiety disorders being the most constant condition.

The likelihood of current psychiatric disorders was associated with age (odds ratio [OR] 0.97; 95 % confidence interval [CI] 0.95–0.99) and years of education (OR=0.92; 95 % CI 0.86–0.98). No evident predictors were associated with lifetime disorders. Correctly classified cases accounted for 57.8 % of current disorders, and 80.9 % of lifetime disorders (Table 4).

Discussion

In our sample, almost two-thirds of obese bariatric surgery candidates met the criteria for any current psychiatric

disorders, and four out of five for any lifetime psychiatric disorder. The most prevalent and stable class of current diagnosis was anxiety disorder. Among lifetime disorders, mood disorders were ranked as most prevalent, with bipolar disorders being the most common lifetime mood conditions. The study assessed reliably the psychiatric diagnosis of a large sample of obese patients before undertaking bariatric surgery, in contrast to limited sample size of some previous studies [29–32, 34]. Besides the structured interview (SCID-I), the level of overall functioning (GAF) due to psychopathology also was evaluated.

High rates of psychiatric disorders among candidates for bariatric surgery seem to be the rule rather than an exception. Comparing with studies adopting similar methodology, the lifetime rates have shown similar high prevalence of psychopathology. The rates ranged from 36.8 to 72.6 % for lifetime disorders in studies reported in USA [29–31] and Europe [32, 34]. Our rate was slightly higher than previous studies, and some difference of prevalence rates in these studies might be attributable to their methods, such as in-person interview [31, 32, 34] vs. telephone interview [30], or mandatory mental assessment in pre-surgical period as requirement for surgery [29, 34]. Therefore, the validity of our findings should be considered in view of reliable strategy of psychiatric assessment, without coupling the evaluation with the surgery schedule, and high participation rate. In comparison, only the non-Western study [5] reported a lower rate of 54.1 % among surgical obese patients. Besides methodological differences, ethnicity might partly explain this variation.

The prevalence of psychiatric diagnosis among our sample is at least twice to that of the rates found in general population, which has a 12-month prevalence ranging from 4.3 to 29.6 % [44]. Also, the frequent occurrence of bipolar disorders in obese samples should be underlined, outnumbering major depressive disorders [23, 45]. When compared with rates found in general population, the bipolarity is an outstanding feature found in our sample, except for an Italian study [33], which assessed bipolar spectrum disorders.

The majority of participants of studies assessing pre-surgery psychopathology were women [5, 29–32, 34], but the average BMI of men was significantly higher in our sample. The comorbidity rate was similar between men and women, and comparable results were found in a North American study [29]. Conversely, Muhlans and colleagues [32] have found that women had more comorbidities than men. Although gender difference in the prevalence of psychiatric disorders was reported in general population [44, 46], these findings could not replicate in all pre-surgical studies on obesity [30, 31, 34]. However, some studies found gender difference in their rates of psychiatric disorders [5, 29, 32] and

specific disorders also showed differences, for example, eating disorder [32], major depressive disorder, and anxiety disorders [28]. Explanations for this difference are gender-specific illness behavior and help-seeking habits that might be shaped by societal pressure of thinness.

Similarly to previous findings [33], younger age and those less-educated people emerged as a population strata with increased risk of mental health disorders, albeit this result could not always be confirmed by similar studies [32]. Future studies should draw attention to most vulnerable population to implement universal preventive programs, such as for the childhood obesity and healthy lifestyle habits.

Some limitations of our study should be noted. First, the patients were recruited without control subjects from a single hospital in Southeast Brazil, which can impede the generalizability of findings to other Brazilian regions. This bariatric center is located in a large metropolitan area with characteristics of developed countries, where around 10 % of the Brazilian population lives, but with large ethnic heterogeneity [47].

Even the assessments were conducted blindly and independently to the pre-surgical screening and the scheduled date of the surgical procedure; the social desirability bias might have affected the patients. Possibly, many patients have not disclosed problems fearing that results of the assessment might lead to the disapproval or delay of surgery, leading to underestimation of psychiatric disorders. Conversely, exaggerating their symptoms could serve to bypass their ranking in the waiting list. This phenomenon of impression management is well-recognized in a sound literature among bariatric patients and professionals [48–53], downward affecting the true frequency of psychopathology [31, 54].

In the case of extreme obese individuals (BMI>50), mobility difficulties might have an influence in the decision to decline their participation. These subjects might have reduced the actual prevalence of psychiatric disorder in the sample, since it is expected that they present more severe psychopathologies.

This investigation provides evidence that psychiatric disorders are prominent attribute of class III obesity seeking bariatric surgery and highlight the importance of using standardized diagnostic tools for psychiatric diagnosis in pre-surgical obese patient population, allowing further comparison and follow-up. It is recommended that obese patients be systematically assessed during the pre-surgery period [55], in relation to the occurrence of psychiatric disorders in addition to clinical and nutritional evaluation.

Future studies in Latin America should confirm the short-term and long-term effects of bariatric surgery on mental

health condition of these patients [56–58], as well as to contribute to understand the causal relationship between obesity and psychiatric disorders [9, 13, 59, 60].

Conflict of Interest The investigation received grant from the Foundation for Research Support of the State of São Paulo (FAPESP # 2012/17435-7); Y.-P. W. is the recipient of this grant. L. S. D. G. received a scholarship from the Foundation for Research Support of the State of São Paulo (FAPESP# 2012/17498-9). B. M. C. and M. A. S. declare no conflict of interest.

Statement of Informed Consent Informed consent was obtained from all individual participants included in the study.

Statement of Human and Animal Rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The ethics committee of the University of São Paulo Medical School approved the study.

References

- Global Burden of Metabolic Risk Factors for Chronic Diseases C, Lu Y, Hajifathalian K, et al. Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1.8 million participants. *Lancet*. 2014;383:970–83.
- Prince M, Patel V, Saxena S, et al. No health without mental health. *Lancet*. 2007;370:859–77.
- Abegunde DO, Mathers CD, Adam T, et al. The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet*. 2007;370:1929–38.
- Wang YC, McPherson K, Marsh T, et al. Health and economic burden of the projected obesity trends in the USA and the UK. *Lancet*. 2011;378:815–25.
- Lin HY, Huang CK, Tai CM, et al. Psychiatric disorders of patients seeking obesity treatment. *BMC Psychiatry*. 2013;13:1.
- Suzuki J, Haimovici F, Chang G. Alcohol use disorders after bariatric surgery. *Obes Surg*. 2012;22:201–7.
- Scott KM, McGee MA, Wells JE, et al. Obesity and mental disorders in the adult general population. *J Psychosom Res*. 2008;64:97–105.
- Simon GE, Von Korff M, Saunders K, et al. Association between obesity and psychiatric disorders in the US adult population. *Arch Gen Psychiatry*. 2006;63:824–30.
- National Obesity Observatory- NOO. International comparisons of obesity prevalence. Association of public health observatories: 2011.
- National Heart Lung and Blood Institute. North American association for the study of obesity. The practical guide identification, evaluation, and treatment of overweight and obesity in adults. NIH publication no 00-4084. Bethesda: The Institute; 2000.
- Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. *Nutr Rev*. 2012;70:3–21.
- Rodgers GP, Collins FS. The next generation of obesity research: no time to waste. *Jama*. 2012;308:1095–6.
- Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry*. 2010;67:220–9.
- Janssen I. The public health burden of obesity in Canada. *Canadian J Diab*. 2013;37:90–6.
- Wolf AM, Colditz GA. Social and economic effects of body weight in the United States. *Am J Clin Nutr*. 1996;63:466S–69S.
- Odegaard K, Borg S, Persson U, et al. The Swedish cost burden of overweight and obesity—evaluated with the PAR approach and a statistical modelling approach. *Int Jediat Obesity IJPO Off J Int Assoc Stud Obesity*. 2008;3 Suppl 1:51–7.
- Wijnhoven TM, van Raaij JM, Spinelli A, et al. WHO European childhood obesity surveillance initiative 2008: weight, height and body mass index in 6–9-year-old children. *Pediatr Obesity*. 2013;8:79–97.
- Malik S, Mitchell JE, Engel S, et al. Psychopathology in bariatric surgery candidates: a review of studies using structured diagnostic interviews. *Compr Psychiatry*. 2014;55:248–59.
- World Health Organization - WHO. Global status report on noncommunicable diseases 2010. Description of the global burden of NCDs, their risk factors and determinants. In: WH Organization, editor. Global status report on noncommunicable diseases 2010. Geneva: World Health Organization; 2011. p. 176.
- Uauy R, Albala C, Kain J. Obesity trends in Latin America: transiting from under- to overweight. *J Nutr*. 2001;131:893S–99S.
- Du SF, Lu B, Zhai FY, et al. A new stage of the nutrition transition in China. *Public Health Nutr*. 2002;5:169–74.
- Monteiro CA, Conde WL, Popkin BM. Is obesity replacing or adding to undernutrition? Evidence from different social classes in Brazil. *Public Health Nutr*. 2002;5:105–12.
- Schmidt MI, Duncan BB, Azevedo e Silva G, et al. Chronic non-communicable diseases in Brazil: burden and current challenges. *Lancet*. 2011;377:1949–61.
- Sociedade brasileira de cirurgia bariátrica e Metabólica - SBCBM. Mapeamento obesidade. 2007. In: <http://www.scbm.org.br/wordpress/>.
- North American Association for Study of Obesity - NAASO. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. Bethesda: National Institutes of Health; 1998.
- Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *Jama*. 2004;292:1724–37.
- Portal da saúde-ministério público. Total de cirurgias de redução de estômago sobe 542%. In: Saúde Md (ed.): Portal da Saúde 2009.
- Rosenberg SD, Lu WL, Mueser KT, et al. Correlates of adverse childhood events among adults with schizophrenia spectrum disorders. *Psychiatr Serv*. 2007;58:245–53.
- Rosenberger PH, Henderson KE, Grilo CM. Psychiatric disorder comorbidity and association with eating disorders in bariatric surgery patients: a cross-sectional study using structured interview-based diagnosis. *J Clin Psychiatry*. 2006;67:1080–5.
- Kalarchian MA, Marcus MD, Levine MD, et al. Psychiatric disorders among bariatric surgery candidates: relationship to obesity and functional health status. *Am J Psychiatry*. 2007;164:328–34. quiz 74.
- Mitchell JE, Selzer F, Kalarchian MA, et al. Psychopathology before surgery in the longitudinal assessment of bariatric surgery-3 (LABS-3) psychosocial study. *Surg Obesity Relat Dis Off J Am Soc Bariat Surg*. 2012;8:533–41.
- Muhlans B, Horbach T, de Zwaan M. Psychiatric disorders in bariatric surgery candidates: a review of the literature and results of a German prebariatric surgery sample. *Gen Hosp Psychiatry*. 2009;31:414–21.
- Alciati A, D'Ambrosio A, Foschi D, et al. Bipolar spectrum disorders in severely obese patients seeking surgical treatment. *J Affect Disord*. 2007;101:131–8.
- Mauri M, Rucci P, Calderone A, et al. Axis I and II disorders and quality of life in bariatric surgery candidates. *J Clin Psychiatry*. 2008;69:295–301.
- Petribu K, Ribeiro ES, Oliveira FMF, et al. Transtorno da compulsão alimentar periódica em uma população de obesos mórbidos candidatos a cirurgia bariátrica do hospital universitário Oswaldo Cruz, em Recife - PE. *Arquivos Brasileiros de Endocrin Metabol*. 2006;50:901–08.

36. Rojas C, Brante M, Miranda E, et al. Anxiety, depression and self-concept among morbid obese patients before and after bariatric surgery. *Revista Medica De Chile*. 2011;139:571–78.
37. First MB, Spitzer RL, Gibbon M, et al. Structured clinical interview for DSM-IV-TR axis I disorders, research version, patient edition. (SCID-I/P) New York: biometrics research. New York: New York State Psychiatric Institute; 2002.
38. American Psychiatry Association - APA. Manual diagnóstico e estatístico de transtornos mentais, texto revisado - DSM-IV-Tr. 4th ed. Washington DC: American Psychiatry Association; 2000.
39. Del-Ben CM, Rodrigues CR, Zuairi AW. Reliability of the Portuguese version of the structured clinical interview for DSM-III-R (SCID-I) in a Brazilian sample of psychiatric outpatients. *Brazilian J Med Biol Res Revista Brasileira de Pesquisas Med Biol Soc Brasileira de Biofísica*. 1996;29:1675–82.
40. Aas IH. Global assessment of functioning (GAF): properties and frontier of current knowledge. *Ann Gen Psychiat*. 2010;9:20.
41. Hall RC. Global assessment of functioning. A modified scale. *Psychosomatics*. 1995;36:267–75.
42. Cohen J, Fleiss J. The equivalence of weighted kappa and the intraclass correlation coefficient as measures of reliability. *Educ Psychol Meas*. 1973;33:613–19.
43. Inc S. PASW statistics for windows. SPSS Inc. Chicago: SPSS Inc; 2009.
44. Demyttenaere K, Bruffaerts R, Posada-Villa J, et al. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization world mental health surveys. *Jama*. 2004;291:2581–90.
45. Litwack SD, Mitchell KS, Sloan DM, et al. Eating disorder symptoms and comorbid psychopathology among male and female veterans. *Gen Hosp Psychiatry*. 2014;36:406–10.
46. Andrade LH, Wang YP, Andreoni S, et al. Mental disorders in megacities: findings from the Sao Paulo megacity mental health survey. *Brazil PLoS One*. 2012;7:e31879.
47. Instituto brasileiro de geografia e estatística - IBGE. Contagem da população 2007 tabelas.: Sistema IBGE de Recuperação Automática—SIDRA. 2007.
48. Fabricatore AN, Wadden TA, Womble LG, et al. The role of patients' expectations and goals in the behavioral and pharmacological treatment of obesity. *Int J Obes*. 2007;31:1739–45.
49. Fabricatore AN, Crerand CE, Wadden TA, et al. How do mental health professionals evaluate candidates for bariatric surgery? *Surv Res Obesity Surg*. 2006;16:567–73.
50. Mitchell JE, Steffen KJ, de Zwaan M, et al. Congruence between clinical and research-based psychiatric assessment in bariatric surgical candidates. *Surg Obes Relat Dis*. 2010;6:628–34.
51. O'Neal KS, Crosby KM. Patients' perceptions of a pharmacist-managed weight management clinic in a community setting. *Res Social Admin Pharm*. 2013;9:129–36.
52. Walfish S, Brown TA. Patient expectations of weight loss from bariatric surgery. *Bariatric Nurs Surg Pat Care*. 2006;1:205–10.
53. Walfish S, Vance D, Fabricatore AN, et al. Psychological evaluation of bariatric surgery applicants: procedures and reasons for delay or denial of surgery. *Obes Surg*. 2007;17:1578–83.
54. Mitchell JE, Crosby R, de Zwaan M, et al. Possible risk factors for increased suicide following bariatric surgery. *Obesity*. 2013;21:665–72.
55. Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient-2013 update: cosponsored by American association of clinical endocrinologists, the obesity society, and american society for metabolic & bariatric surgery. *Obesity*. 2013;21:S1–S27.
56. de Zwaan M, Enderle J, Wagner S, et al. Anxiety and depression in bariatric surgery patients: a prospective, follow-up study using structured clinical interviews. *J Affect Disord*. 2011;133:61–8.
57. Wadden TA, Faulconbridge LF, Jones-Corneille LR, et al. Binge eating disorder and the outcome of bariatric surgery at one year: a prospective. *Observational study*. *Obesity*. 2011;19:1220–28.
58. Jones-Corneille LR, Wadden TA, Sarwer DB, et al. Axis I psychopathology in bariatric surgery candidates with and without binge eating disorder: results of structured clinical interviews. *Obes Surg*. 2012;22:389–97.
59. Herva A, Laitinen J, Miettunen J, et al. Obesity and depression: results from the longitudinal Northern Finland 1966 Birth Cohort study. *Int J Obes*. 2006;30:520–27.
60. Goodman E, Whitaker RC. A prospective study of the role of depression in the development and persistence of adolescent obesity. *Pediatrics*. 2002;110:497–504.

B. **Duarte-Guerra LS**, Gorenstein C, Paiva-Medeiros PF, Santo MA, Lotufo Neto F, Wang YP. Clinical utility of the Montgomery-Åsberg Depression Rating Scale for the detection of depression among bariatric surgery candidates. *BMC Psychiatry*. 2016 Apr 30;16:119. doi: 10.1186/s12888-016-0823-8.

Permission for reuse by BMC Psychiatric from SpringerNature.

RESEARCH ARTICLE

Open Access

Clinical utility of the Montgomery-Åsberg Depression Rating Scale for the detection of depression among bariatric surgery candidates

Leorides Severo Duarte-Guerra¹, Clarice Gorenstein^{1,2}, Paula Francinelle Paiva-Medeiros¹, Marco Aurélio Santo³, Francisco Lotufo Neto¹ and Yuan-Pang Wang^{1,4*}

Abstract

Background: Clinical assessment of depression is an important part of pre-surgical assessment among individuals with morbid obesity. However, there is no agreed-upon instrument to identify mood psychopathology in this population. We examined the reliability and criterion validity of the clinician-administered Montgomery-Åsberg Depression Rating Scale (MADRS) and the utility of a short version for bariatric surgery candidates.

Methods: The sample was 374 patients with obesity, consecutively recruited from the waiting list of a bariatric surgery clinic of University Hospital, Brazil: women 80 %, mean BMI 47 kg/m², mean age 43.0 years. The 10-item MADRS was analyzed against the SCID-I. Items that showed small relevance to sample's characteristics and contribution to data variability were removed to develop the short 5-item version of scale. We calculated the sensitivity and specificity of cutoff points of both versions MADRS, and values were plotted as a receiver operating characteristic curve.

Results: For the 10-item MADRS, the Cronbach's alpha coefficient was 0.93. When compared against SCID-I, the best cut-off threshold was 13/14, yielding sensitivity of 0.81 and specificity 0.85. Following items were removed: reduced appetite, reduced sleep, concentration difficulties, suicide thought and lassitude. The 5-item version showed an alpha coefficient of 0.94 and a best cut-off threshold of 10/11, yielding sensitivity of 0.81 and specificity 0.87. Similar overall ability to discriminate depression of almost 90 % was found for both 10-item and 5-item MADRS.

Conclusion: The MADRS is a reliable and valid instrument to assess depressive symptoms among treatment-seeking bariatric patients. Systematic application of the abbreviated version of the MADRS can be recommended for enhancing the clinical detection of depression during perioperative period.

Keywords: Obesity, Depression, Psychopathology, Bariatric surgery

* Correspondence: gnep_inbox@hotmail.com

¹Department and Institute of Psychiatry (LIM-23), University of São Paulo Medical School, São Paulo, Brazil

⁴Instituto & Departamento de Psiquiatria, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo, Rua Dr. Ovídio Pires de Campos. no. 785, 05403-010 São Paulo, Brazil

Full list of author information is available at the end of the article

© 2016 Duarte-Guerra et al. **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

Background

Depression and obesity are onerous non-communicable conditions that frequently coexist [1]. Depressive disorder is one of the most common psychiatric comorbidities among patients with severe obesity ($\text{BMI} > 40 \text{ kg/m}^2$), in the pre- and the post-surgical period [2, 3]. Potential bidirectional relationship between obesity and depression is observed and possible causal relationship between these conditions is suggested [4]. Although pre-surgery depression alone has not been shown to be a robust outcome predictor of post-operative weight loss [5], its presence in pre-surgical period can contraindicate bariatric procedure [6]. Therefore, the accurate identification of psychopathology is a crucial step in these patients.

Most of bariatric clinicians acknowledge that depression should be treated and stabilized before surgery, but there are problems in its detection. Non-recognition of depressive symptoms can result in misdiagnosis [7] and unreliable judgment of surgical eligibility [8]. Moreover, many patients tend to present themselves in positive light during psychosomatic evaluations, highlighting somatic symptoms to meet medical expectations and clinical guidelines of pre-surgical assessment. This impression management represents an effort to control or influence the perceptions of healthcare staff in the approval process [6, 9].

The performance of symptomatic scales of depression can be altered when somatic and cognitive symptoms co-occur alongside of depressive symptoms [9], what can also lead to misclassification and mistakes in surgical indication. While overdetected depression can increase disapprovals to bariatric surgery [6, 9], its underdetection can cause unfavorable outcome among unrecognized depressive patients in post-surgical periods [10]. Thus, the adoption of accurate methods displaying acceptable sensitivity and specificity to identify perioperative psychopathology can reduce the burden of depression among bariatric patients [11].

Some popular instruments for detection of depression were used in this population, e.g., the Hamilton Depression Rating Scale – HAM-D [12, 13], the Beck Depression Inventory – BDI [9, 14–20], the Hospital Anxiety and Depression Scale – HADS [21–23], and the Patient Health Questionnaire – PHQ [20, 24, 25]. Most of tools are self-administered for screening depression and some researchers claim that these scales are conceptually flawed for use in specific settings and patients [9, 13, 26], with several psychometric limitations (e.g., poor reliability or validity) unsuitable to determine bariatric surgery.

Among available self-report scales, the BDI is the most common one reported with the purpose of pre-surgical screening for depression among obese populations [9, 15–20]. However, self-reporting instruments like the BDI yield low level of depressive symptoms and significant proportion of false-positive cases [15],

due to patient's characteristics and response style in bariatric setting during preoperative assessment [9]. The HADS does not include somatic symptoms and is viewed as an easy tool to administer in this population; this instrument has been adopted as indicator of psychopathology in a large prospective Swedish Obese Subjects (SOS) trial [22]. Nevertheless, its applicability can be questioned for discriminating depressive illness, as this tool has presented low sensitivity among breast cancer participants [26].

Structured clinician-administered scales for depression have not been well studied in bariatric population. In comparison to the HAM-D, the Montgomery–Åsberg Depression Rating Scale – MADRS [27] encompasses limited number of somatic symptoms. Moreover, the decision for choosing MADRS instead of HAM-D eventually rest on consensus that a useful instrument should capture adequately the construct of depression among patient samples [11], with empirical evidence of psychometric robustness and cost-effectiveness [28].

Given the need for standardized assessment tools that have validity evidence in bariatric population and clinician-administered scales for depression have not been well studied in this population, we investigated the applicability of the MADRS for a sample of pre-surgical patients in the waiting list of a bariatric clinic. The MADRS has never been applied to preoperative bariatric candidates and incorporates a structured interview embedded in a brief 10-item scale [29]. We aimed to determine the accuracy of the scale (a) to estimate its reliability and validity for assessing depression, and (b) to test whether it is possible to develop a short version of instrument without somatic-cognitive symptoms.

Methods

This validation study determined the performance of the MADRS for assessing depression among patients seeking bariatric surgery.

Sampling and recruitment

The participants were recruited from a University-based bariatric center in Brazil and should meet the criteria of class III obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$) or class II ($\text{BMI} \geq 35 \text{ kg/m}^2$) with medical comorbidities. They were ranked in a waiting list in accordance to admission date in the program and clinical severity.

The first 500 eligible patients in the list were consecutively invited by telephone to participate in the study. After brief explanation, 63 patients declined to participate. Additional 63 patients were excluded during the assessment period due to: severe psychiatric illness ($n = 2$), previous bariatric surgery ($n = 5$), mobility difficulty ($n = 37$), and incomplete interviews ($n = 19$). The final sample was

comprised of 374 individuals, with a participation rate of 74.8 %.

Table 1 shows the demographic characteristics of participants. Of 374 participants, the majority were women (79.9 %). Regarding marital status, half of them were married/cohabiting (50.8 %), one-quarter was single (25.4 %), the remaining was separated/divorced (16.8 %) or widowed (7.0 %). The mean schooling was 9.6 years of education (standard deviation [SD] 3.5), being 35.6 % with 8 years and 44.9 % with 11 years. The mean age was 43.0 years (SD 11.6) and the mean BMI was 47.0 kg/m² (SD 7.1; range 31.2–92.1).

Instruments

- a) Montgomery-Åsberg Depression Rating Scale (MADRS) [27] investigates the presence of affective, somatic, cognitive and behavioral symptoms of depression. Ten symptoms are rated on a 0–6 scale, along the possible scores of 0–60. The total score classifies the patients in levels of severity: normal or absent 0–6; mild 7–19; moderate 20–34; and severe 35–60 [30]. We used the Portuguese version of MADRS [31] with the aid of the Structured Interview Guide for the MADRS (SIGMA) [29] to assess the anchor points of each item. The raters were clinical psychologists with experience in bariatric patients, whose scores were calibrated in 3 consensus meetings. Previous psychometric study [32] reported the intraclass correlation coefficient (ICC) of the MADRS as acceptable for unipolar depression, ranging between 0.83 and 0.86. These interviewers were blind to patients' psychiatric diagnosis and rated independently depressive

symptoms from November 2010 to March 2012, totaling 17 months. The duration of the SIGMA ranged from 10 to 40 min, without refusal.

- b) Structured Clinical Interview for DSM-IV Axis I Disorder (SCID-I) [33] is a standardized semi-structured interview generally accepted as gold standard to make diagnosis of psychiatric disorders [34]. From 2010 to 2012, participants were randomly assigned to be face-to-face assessed by trained psychologists with previous experience in obesity and bariatric surgery, with an inter-rater *kappa* estimated as 0.81 [35]. The duration of the interview ranged from 60 to 90 min for the SCID-I. The psychiatric diagnoses of this sample can be inspected in Additional file 1: Table S1.

Statistical analysis

Descriptive analysis depicted mean MADRS item endorsement rate, standard deviation (SD) and range. The Pearson's coefficient of variation (CV), Cronbach's alpha coefficient (α) and item commonality (h^2) were calculated for each item and total score. Non-relevant symptoms were eliminated in accordance with following rationale: (a) clinic wisdom, (b) item endorsement and (c) commonality values. To inspect the between-variable structure of correlation, the dimensionality of the MADRS was examined through factor analysis [36].

Subsequently, the signal detection analysis was performed to establish the best cut-off point by adopting the diagnosis of SCID-I/DSM-IV major depressive disorder as gold standard. The sensitivity and specificity, the positive and negative predictive values (PPV/NPV) were calculated for all possible thresholds. The Youden's index (γ) [37] was calculated to summarize the overall misclassification. The Receiver Operating Characteristic (ROC) curve was built by plotting data of sensitivity and false-positive rates. The values of Area Under the Curve (AUC) and their respective 95 % confidence intervals (CI) were calculated.

All analyses were performed using SPSS version 20.0 and the level of significance was set at $p < 0.05$ for two-tailed tests.

Results

Among 374 participants, 7 % ($N = 26$) met the criteria for major depressive episode and 27.5 % ($N = 103$) lifetime major depression in accordance with SCID-I/DSM-IV criteria. The mean total score of MADRS was 7.73 (SD 11.33, range 0–58, CV 1.47). The highest item endorsement rates (mean score around 1.0) were observed for 'apparent sadness', 'reduced sleep', 'reported sadness' and 'inner tension'. The lowest endorsement rates (mean < 0.75) were 'suicidal thoughts', 'reduced appetite', 'pessimistic thoughts' and 'concentration difficulties'.

Table 1 Demographic characteristics of the sample ($n = 374$)

Characteristic	N	(%)
Sex		
Female	299	79.9
Male	75	20.1
Marital status		
Married/cohabiting	190	50.8
Single	95	25.4
Separated/divorced	63	16.8
Widowed	26	7.0
Education		
8 years	133	35.6
11 years	168	44.9
15 years +	73	19.5
Mean age, years (S.D.)	43.0 (11.6)	
Mean BMI, kg/m ² (S.D.)	47.0 (7.1)	

The items with the highest dispersion ($CV > 2.0$) were 'suicidal thoughts', 'reduced appetite' and 'pessimistic thoughts', indicating sizable response bias of score precision (Table 2). Although women scored higher than men (8.08 vs. 6.33), high data dispersion has cancelled the statistical difference between sexes ($p = 0.23$).

For the 10-item scale, the Cronbach's alpha coefficient was 0.93, showing adequate homogeneity. Item-total correlation demonstrated that deleting any item would affect slightly the internal consistency of the construct (Cronbach's alpha range 0.92–0.94). Conversely, the analysis of commonalities indicated that following somatic-cognitive items explained smaller proportion of data variability ($h^2 < 0.7$), in decreasing order: 'reduced appetite', 'reduced sleep', 'suicidal thoughts', 'concentration difficulties' and 'lassitude'.

The sensitivity, specificity, PPV, NPV and best cut-off point for scores of the 10-item and 5-item MADRS are presented in Table 3. For 10-item MADRS, the best trade-off threshold between sensitivity and specificity was 13/14, yielding sensitivity 0.85 and specificity 0.81. The PPV and NPV were 0.70 and 0.91, respectively. The highest Youden's index was $\gamma = 0.66$. Further analysis showed that 23.8 % of participants scored above 13 points with mean score of 24.96 (25.1 % women and 18.7 % men).

The factor analysis demonstrated a unidimensional structure of 'general depression' for MADRS, explained 63.4 % of data variability and salient factor loadings > 0.4 in all items (not shown). Because 'reduced appetite', 'reduced sleep' and 'suicidal thoughts' showed lower commonalities ($h^2 < 0.5$), and 'concentration difficulties' and

'lassitude' showed moderate commonalities ($h^2 < 0.7$), these somatic-cognitive items were sequentially removed to develop short versions of scale. While 'pessimistic thoughts' presented high CV of 2.14, its contribution to the underlying construct was substantial ($h^2 = 0.74$) and was retained in the final version.

The 5-item version presented Cronbach's alpha of 0.94 and showed comparable performance with 10-item version, in terms of sensitivity and specificity (Table 3). For the best threshold of 10/11, 19.0 % of the sample scored above 10 points (19.4 % women and 17.3 % men).

The sensitivity and false-positive rates ($1 - \text{specificity}$) were used to construct the ROC curve (Fig. 1). The area under the curve (AUC) of 0.87 showed that the discriminative accuracy of scale was satisfactory for both 10-item and 5-item versions. Their respective CI95 % of 0.82–0.92 and 0.81–0.93 indicated substantial overlap between two versions of the scale. In summary, these acceptable results indicated that the MADRS was appropriated for the detection of depression.

Discussion

Widely adopted in follow-up studies and clinical trials in medical samples it is the first time that the applicability of MADRS was psychometrically investigated among patients with severe obesity. We have shown that the MADRS could be used with good confidence, high sensitivity and specificity in this population. Also, this clinician-administered scale could be customized into a short version, preserving robust psychometric properties. Accurate detection of depression and proper indication of individuals to surgical intervention present a potential impact for public health.

The majority of psychometric studies investigating MADRS confirm its satisfactory reliability, with Cronbach's alpha close to 0.8 and over [38]. Reliable pre-operative evaluations may ensure the reproducibility of pre-operative assessments and improve post-operative outcomes [6, 8].

Where to place the cut-off point to determine the presence of relevant depressive symptoms is critical to the domain of public health. Among clinical studies on MADRS, researchers reported the best threshold ranging from 6 to 21. The large range of cut-off scores indicates the need of validity investigation to ensure its applicability for specific populations. Similar to present study, three studies reported the best cut-off of 13/14 [39] for neurodegenerative patients, one study recommended 6/7 for bipolar patients [40] and another 20/21 for geriatric sample [41].

Concerning the severity level of depression, the mean score of 7.7 could detect cases of "mild depression" [30]. Highly sensitive threshold of 6/7 can be recommended for screening purpose in community studies.

Table 2 Mean, standard deviation (SD), coefficient of variation (CV) of the Montgomery-Åsberg Depression Rating Scale (MADRS) for severely obese patients ($N = 374$). Item-total correlation and commonalities

Item	Mean	SD	CV	α	h^2
Apparent sadness	1.10	1.70	1.55	0.92	0.79
Reported sadness	0.99	1.72	1.74	0.92	0.77
Inner tension	0.94	1.47	1.56	0.92	0.71
Reduced sleep	1.00	1.63	1.63	0.93	0.41
Reduced appetite	0.48	1.08	2.25	0.94	0.33
Concentration difficulties	0.74	1.39	1.88	0.93	0.62
Lassitude	0.76	1.38	1.82	0.92	0.67
Inability to feel	0.76	1.45	1.91	0.92	0.81
Pessimistic thoughts	0.63	1.35	2.14	0.92	0.74
Suicidal thoughts	0.33	0.99	3.00	0.93	0.49
Total	7.73	11.33	1.47	0.93	0.63 ^a

CV Pearson's coefficient of variation = $SD/Mean$

α Cronbach's alpha coefficient of internal consistency

h^2 Commonality

^aTotal percentage of data explained by unidimensional model of the MADRS

Table 3 Sensitivity, specificity, positive and negative predictive values (PPV and NPV) and best cut-off point for scores of the 10-item and 5-item MADRS

10-item MADRS											
Cut-off	5/6	6/7	7/8	8/9	9/10	10/11	11/12	12/13	13/14^a	14/15	15/16
Sensitivity	0.92	0.92	0.92	0.90	0.87	0.85	0.85	0.85	0.85	0.77	0.69
Specificity	0.64	0.66	0.69	0.70	0.74	0.76	0.77	0.81	0.81	0.83	0.84
PPV	0.52	0.56	0.56	0.57	0.59	0.60	0.62	0.69	0.70	0.72	0.72
NPV	0.95	0.95	0.95	0.94	0.93	0.92	0.92	0.91	0.91	0.86	0.82
γ	0.56	0.58	0.61	0.62	0.62	0.61	0.62	0.66	0.66	0.60	0.53
5-item MADRS											
Cut-off	5/6	6/7	7/8	8/9	9/10	10/11^a	11/12	12/13	13/14	14/15	15/16
Sensitivity	0.88	0.88	0.85	0.81	0.81	0.81	0.69	0.65	0.58	0.58	0.46
Specificity	0.75	0.76	0.81	0.85	0.86	0.87	0.88	0.90	0.90	0.90	0.93
PPV	0.57	0.56	0.61	0.70	0.71	0.75	0.74	0.78	0.76	0.76	0.81
NPV	0.71	0.94	0.94	0.91	0.91	0.90	0.85	0.82	0.79	0.79	0.72
γ	0.63	0.64	0.66	0.66	0.67	0.68	0.57	0.55	0.48	0.48	0.47

γ Youden's index = (sensitivity + specificity) - 1

^aMaximum trade-off between sensitivity and specificity

Bold-data: MADRS' threshold scores

Examining the threshold region between 6 and 9, the scale still has detected cases of depression with substantial sensitivity. However, the specificity of approximately 70 % along with lower PPV (<0.6) was of limited help to identify active cases of depression. While the sensitivity has slightly reduced in the region between 10 and 14, substantial improvement in specificity was observed. The recommended threshold for patients with severe obesity should be 13/14 (mean score around 25), where cases were classified as "moderate depression" with higher specificity. This versatile performance of MADRS

can refer cases with different level of depression and settings, for example, in pre-surgical period.

The clinician should be mindful of the disease and sample's characteristics to interpret the scores of MADRS. The tolerable number of cases of false-positives or false-negatives should be taken into account. Particularly, the low endorsement rate of 'reduced appetite' in patients with obesity indicates that this symptom can decrease the total score and the identification of depression in over-eating individuals. Similarly, the inclusion of 'suicidal ideation', which is infrequently observed among high BMI

Fig. 1 Receiver operating characteristics (ROC) curve and Area Under Curve (AUC) of the 10-item and 5-item MADRS for severely obese patients (N = 374)

individuals [42], can lead to inconsistent assessment. If these symptoms are included in the scale, many depressed patients will go unnoticed and remain false-negative cases, even they present clinical depression.

Clinical characteristics associated with obesity may obscure the pattern of reported symptoms by this medical population [43]. For example, obesity-related sleepiness and fatigue are often described by overweight patients and can be misinterpreted as depressive symptom by respondents. Thus, the items 'reduced sleep' and 'lassitude' also was removed in the short version.

Considering the sample's characteristics, most of participants were waiting for years to undertake bariatric surgery. Possibly, these eager patients have inclined to respond to evaluation in order to appear positively appropriate to do so [7]. This illness behavior may have affected the truthfulness of answers to interviews regarding the presence of psychopathology [2]. The supposition that some patients might have exaggerated, disguised or minimized the severity of depressive symptoms is compatible with data dispersion of current investigation. This type of response bias can be minimized with observer scales such as the MADRS and its standardized schedule SIGMA. Possible sex difference affecting the performance of long and short version of the MADRS should be tested in a larger size sample.

Finally, it is advocated that the retention of affective symptoms can effectively identify depressive syndrome with confidence and accuracy with the 5-item version. Somatic-cognitive symptoms of depression should be discarded during preoperative assessment of bariatric patients [39]. The positive acceptance of the short scale by the users, both patients and overloaded clinicians, can increase the cost-effectiveness of assessment for inexpensive implementation in bariatric clinics.

Limitations

Some limitations of this study should be considered before generalizing the results of this investigation to population with severe obesity. All participants were recruited from a single university hospital, raising reservations about the representativeness of participants. However, large sample size and high participation rate support key findings of our data.

Impression management operates among preoperative bariatric patients and alters the results of symptomatic scales and clinical interviews [2, 6, 8]. These patients have produced imprecise responses (large SD and CV indicators), suggesting that most of widely spread deviations from the central tendency was due to their response style. Although we have adopted rigorous SCID-I interview and SIGMA schedule for assessing depression, the social desirability bias can only be minimized, but not completely ruled out [7]. In this context, higher

specificity of the face-to-face MADRS can curb the proneness of false-positive cases observed in self-report scales [9].

Although we have not directly compared competing symptom scales in the same sample, available psychometric indicators have shown that the MADRS outperforms the results of previous studies with the BDI in bariatric patients [9, 15], yielding higher specificity and lower misclassification rate. Detection of 87 % of cases of depression [39] by MADRS seems to have reduced the tendency of bariatric patients to mask their emotional and physical symptoms [44]. Somatic-cognitive complaints may increase the total BDI score, confounding real medical complaints with depressive ones [9] and reducing its clinical utility. In several instances, different methodology of data collection [6] and adaptation of psychometric tools [39] may be crucial to meet some specific features of study population.

Conclusion

Systematic application of an instrument for assessing depression in bariatric sample must be based on current knowledge of patient's illness behavior in clinical setting, taking into account its psychometric utility and empirical strength. Though there is no agreed-upon guideline for assessing depression among patients with severe obesity, formal mental health evaluation with reliable methods before surgical procedure is recommended [11]. In line with the literature, our investigation showed that the assessment of depression among patients with severe obesity is slippery and requires great caution, where independent interviewers should disregard misleading somatic-cognitive symptoms of depression during preoperative assessment of bariatric surgery.

The forecast that both obesity and depression are epidemic conditions that will rise exponentially in next decades challenges their proper identification as a medical task of utmost interest. Both 10-item and 5-item version of MADRS are effective tools in pre-operative bariatric evaluation of depression, but the abbreviated scale which has removed somatic-cognitive characteristics of treatment-seeking individuals can redress intrinsic inadequacies of the original scale. Systematic assessment with short version of MADRS to detect depression, coordinated screening of patient's weight and metabolic indicators are pivotal to enhance perioperative evaluations of patients with obesity and improve their treatment outcome.

Ethics and consent to participate

The Ethics Committee of the University of São Paulo approved the study. All participants have signed an informed consent after the assurance that their participation would not influence the eligibility for surgery. There were no refusals to interviews.

Consent to publish

Not applicable.

Availability of data and materials

All data supporting the findings is contained within the article and the supplementary material.

Additional file

Additional file 1: Table S1. Frequency of current psychiatric diagnosis for severely obese patients, in accordance with Structured Clinical Interview for DSM-IV Axis-I Disorders. Total sample ($N = 374$) and by sex. (DOC 44 kb)

Abbreviations

AUC: area under the curve; BDI: Beck Depression Inventory; BMI: body mass index; CI: confidence interval; CV: coefficient of variation; DSM-IV: Diagnostic and Statistical Manual of mental disorders, fourth edition; h^2 : commonality; HADS: hospital anxiety and depression scale; HAM-D: Hamilton Depression Rating Scale; ICC: intraclass correlation coefficient; MADRS: Montgomery-Åsberg Depression Rating Scale; NPV: negative predictive value; PHQ: Patient Health Questionnaire; PPV: positive predictive value; ROC: receiver operating characteristics; SCID-I: Structured Clinical Interview for DSM-IV Axis I Disorders; SD: standard deviation; SIGMA: Structured Interview Guide for the MADRS; SOS: Swedish Obese Subjects Trial; SPSS: Statistical Package for the Social Sciences; γ : Youden's Index.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

LSDG and YPW participated in the design of the study, undertook the analysis, interpreted the results and drafted the first version of the article. CG, MAS, FL collaborated with the interpretation of the findings and writing of the article. LSDG and PPM collected data and contributed to writing of the article. All authors approved the final version of the submitted manuscript.

Acknowledgements

None.

Funding

The São Paulo Research Foundation (FAPESP n° 2012/17435-7) funded this investigation. YPW is the recipient of the grant; PPM and LSDG received scholarship from São Paulo Research Foundation (respectively, FAPESP n° 2012/18325-0 and n° 2012/17498-9).

Author details

¹Department and Institute of Psychiatry (LIM-23), University of São Paulo Medical School, São Paulo, Brazil. ²Department of Pharmacology, Institute of Biomedical Sciences, University of São Paulo, São Paulo, Brazil. ³Department of Surgery, University of São Paulo Medical School, São Paulo, Brazil. ⁴Instituto & Departamento de Psiquiatria, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo, Rua Dr. Ovidio Pires de Campos. no. 785, 05403-010 São Paulo, Brazil.

Received: 5 October 2015 Accepted: 21 April 2016

Published online: 30 April 2016

References

- World Health Organization WHO. Obesity and overweight. Media Center, Fact Sheets. Geneva: World Health Organization; 2015. Retrieved from <http://www.who.int/mediacentre/factsheets/fs311/en/>. Accessed 2 Feb 2015.
- Malik S, Mitchell JE, Engel S, Crosby R, Wonderlich S. Psychopathology in bariatric surgery candidates: a review of studies using structured diagnostic interviews. *Compr Psychiatry*. 2014;55:248–59. <http://dx.doi.org/10.1016/j.comppsych.2013.08.021>.
- de Zwaan M, Enderle J, Wagner S, Mühlhans B, Ditzel B, Gefeller O, Mitchell JE, Müller A. Anxiety and depression in bariatric surgery patients: a prospective,

follow-up study using structured clinical interviews. *J Affect Disord*. 2011;133: 61–8. <http://dx.doi.org/10.1016/j.jad.2011.03.025>.

- Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, Zitman FG. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry*. 2010;67:220–9. <http://dx.doi.org/10.1001/archgenpsychiatry.2010.2>.
- Livhits M, Mercado C, Yermilov I, Parikh JA, Dutson E, Mehran A, Ko CY, Gibbons MM. Preoperative predictors of weight loss following bariatric surgery: systematic review. *Obes Surg*. 2012;22:70–89. <http://dx.doi.org/10.1007/s11695-011-0472-4>.
- Fabricatore AN, Crerand CE, Wadden TA, Sarwer DB, Krasucki JL. How do mental health professionals evaluate candidates for bariatric surgery? Survey results. *Obes Surg*. 2006;15:567–73. <http://dx.doi.org/10.1381/096089206776944986>.
- Ambwani S, Boeka AG, Brown JD, Byrne TK, Budak AR, Sarwer DB, Fabricatore AN, Morey LC, O'Neil PM. Socially desirable responding by bariatric surgery candidates during psychological assessment. *Surg Obes Relat Dis*. 2011;9:300–5. <http://dx.doi.org/10.1016/j.soard.2011.06.019>.
- Mitchell JE, Steffen KJ, de Zwaan M, Ertelt TW, Marino JM, Mueller A. Congruence between clinical and research-based psychiatric assessment in bariatric surgical candidates. *Surg Obes Relat Dis*. 2010;6:628–34. <http://dx.doi.org/10.1016/j.soard.2010.01.007>.
- Munoz DJ, Chen E, Fischer E, Roehrig M, Sanchez-Johnson L, Alverdy J, Dymek-Valentine M, le Grange D. Considerations for the use of the Beck Depression Inventory in the Assessment of Weight-Loss Surgery Seeking Patients. *Obes Surg*. 2007;17:1097–01. <http://dx.doi.org/10.1007/s11695-007-9185-0>.
- Kalarchian MA, Marcus MD, Levine MD, Soukalkova JN, Courcoulas AP, Wisinski MS. Relationship of psychiatric disorders to 6-month outcomes after gastric bypass. *Surg Obes Relat Dis*. 2008;4:544–9. <http://dx.doi.org/10.1016/j.soard.2008.03.003>.
- Mechanick JI, Youdim A, Jones DB, Garvey WT, Hurley DL, McMahon MM, Heinberg LJ, Kushner R, Adams TD, Shikora S, Dixon JB, Brethauer S. American Association of Clinical Endocrinologists, Obesity Society, American Society for Metabolic, Bariatric Surgery. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient - 2013 update: cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. *Obesity*. 2013;21 Suppl 1:S1–27. <http://dx.doi.org/10.1002/oby.20461>.
- Hamilton M. Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol*. 1967;6:278–96.
- Bagby RM, Ryder AG, Schuller DR, Marshall MB. The Hamilton Depression Rating Scale: has the gold standard become a lead weight? *Am J Psychiatry*. 2004;161:2163–77. <http://dx.doi.org/10.1176/appi.ajp.161.12.2163>.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4:561–71.
- Hayden MJ, Brown WA, Brennan L, O'Brien PE. Validity of the Beck Depression Inventory as a screening tool for a clinical mood disorder in bariatric surgery candidates. *Obes Surg*. 2012;22:1666–75. <http://dx.doi.org/10.1007/s11695-012-0682-4>.
- Hall BJ, Hood MM, Nackers LM, Azarbad L, Ivan I, Corsica J. Confirmatory factor analysis of the Beck Depression Inventory-II in bariatric surgery candidates. *Psychol Assess*. 2013;25:294–9. <http://dx.doi.org/10.1037/a0030305>.
- Mitchell JE, King WC, Chen JY, Devlin MJ, Flum D, Garcia L, Inabett W, Pender JR, Kalarchian MA, Khandelwal S, Marcus MD, Schroppe B, Strain G, Wolfe B, Yanovski S. Course of depressive symptoms and treatment in the longitudinal assessment of bariatric surgery (LABS-2) study. *Obesity*. 2014;22: 1799–806. <http://dx.doi.org/10.1002/oby.20738>.
- Ayloo S, Thompson K, Choudhury N, Sherifdeen R. Correlation between the Beck Depression Inventory and bariatric surgical procedures. *Surg Obes Relat Dis*. 2015;11:637–42. <http://dx.doi.org/10.1016/j.soard.2014.11.005>.
- Hayes S, Stoeckel N, Napolitano MA, Collins C, Wood GC, Seiler J, Grunwald HE, Foster GD, Still CD. Examination of the Beck Depression Inventory-II Factor Structure Among Bariatric Surgery Candidates. *Obes Surg*. 2015;25:1155–60. <http://dx.doi.org/10.1007/s11695-014-1506-5>.
- Schutt PE, Kung S, Clark MM, Koball AM, Grothe KB. Comparing the Beck Depression Inventory-II (BDI-II) and Patient Health Questionnaire (PHQ-9) Depression Measures in an Outpatient Bariatric Clinic. *Obes Surg*. 2015 [Epub ahead of print].

21. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67:361–70. <http://dx.doi.org/10.1111/j.1600-0447.1983.tb09716.x>.
22. Sjöström L. Review of the key results from the Swedish Obese Subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. *J Intern Med*. 2013;273:219–34. <http://dx.doi.org/10.1111/joim.12012>.
23. Schneck AS, Anty R, Tran A, Hastier A, Amor IB, Gugenheim J, Iannelli A, Piche T. Increased Prevalence of Irritable Bowel Syndrome in a Cohort of French Morbidly Obese Patients Candidate for Bariatric Surgery. *Obes Surg* 2015 Sep 30. [Epub ahead of print].
24. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. *JAMA*. 1999;282:1737–44.
25. Cassin S, Sockalingam S, Hawa R, Wnuk S, Royal S, Taube-Schiff M, Okrainec A. Psychometric Properties of the Patient Health Questionnaire (PHQ-9) as a Depression Screening Tool for Bariatric Surgery Candidates. *Psychosomatics*. 2013;54:352–8. <http://dx.doi.org/10.1016/j.psych.2012.08.010>.
26. Hall A, A'Hern R, Fallowfield L. Are we using appropriate self-report questionnaires for detecting anxiety and depression in women with early breast cancer? *Eur J Cancer*. 1999;35:79–85.
27. Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry*. 1979;134:382–9.
28. Furukawa TA. Assessment of mood: guides for clinicians. *J Psychosom Res*. 2010;68:581–9. <http://dx.doi.org/10.1016/j.jpsychores.2009.05.003>.
29. Williams JB, Kobak KA. Development and reliability of the SIGMA: A structured interview guide for the Montgomery-Åsberg Depression Rating Scale. *Neuropsychopharmacology*. 2006;31:5165–6. <http://dx.doi.org/10.1192/bjp.bp.106.032532>.
30. Hermann N, Black SE, Lawrence J, Szekely C, Szalai JP. The Sunnybrook Stroke Study: A Prospective Study of Depressive Symptoms and Functional Outcome. *Stroke*. 1998;29:618–24. <http://dx.doi.org/10.1161/01.STR.29.3.618>.
31. Dratcu L, da Costa RL, Calil H. Depression assessment in Brazil. The first application of the Montgomery-Åsberg Depression Rating Scale. *Br J Psychiatry*. 1987;150:797–800.
32. Carneiro AM, Fernandes F, Moreno RA. Hamilton Depression Rating Scale and Montgomery-Åsberg Depression Rating Scale in depressed and bipolar I patients: psychometric properties in a Brazilian sample. *Health Qual Life Outcomes*. 2015;13:42. <http://dx.doi.org/10.1186/s12955-015-0235-3>.
33. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV-TR axis I disorders, research version, patient edition. (SCID-I/P). New York: Biometrics Research: New York State Psychiatric Institute; 2002.
34. Shear MK, Greeno C, Kang J, Ludewig D, Frank E, Swartz HA, Hanekamp M. Diagnosis of nonpsychotic patients in community clinics. *Am J Psychiatry*. 2000;157:581–7.
35. Duarte-Guerra LS, Coêlho BM, Santo MA, Wang YP. Psychiatric disorders among obese patients seeking bariatric surgery: results of structured clinical interviews. *Obes Surg*. 2015;25(5):830–7. <http://dx.doi.org/10.1007/s11695-014-1464-y>.
36. Johnson RA, Wichern DW. Applied multivariate statistical analysis. Essex: Pearson Education Limited; 2014.
37. Youden WJ. Index for rating diagnostic tests. *Cancer*. 1950;3:32–5.
38. Bunevicius A, Staniute M, Brozaitiene J, Pommer AM, Pop VJ, Montgomery SA, Bunevicius R. Evaluation of depressive symptoms in patients with coronary artery disease using the Montgomery-Åsberg Depression Rating Scale. *Int Clin Psychopharmacol*. 2012;27:49–55. <http://dx.doi.org/10.1097/YIC.0b013e328357670d>.
39. Reijnders JS, Lousberg R, Leentjens AF. Assessment of depression in Parkinson's disease: the contribution of somatic symptoms to the clinimetric performance of the Hamilton and Montgomery-Åsberg rating scales. *J Psychosom Res*. 2010;68:561–5. <http://dx.doi.org/10.1016/j.jpsychores.2009.10.006>.
40. Riedel M, Moller HJ, Obermeier M, Schennach-Wolff R, Bauer M, Adli M, Kronmüller K, Nickel T, Brieger P, Laux G, Bender W, Heuser I, Zeiler J, Gaebel W, Seemüller F. Response and remission criteria in major depression - a validation of current practice. *J Psychiatry Res*. 2010;44:1063–8. <http://dx.doi.org/10.1016/j.jpsychores.2010.03.006>.
41. Mottram P, Wilson K, Copeland J. Validation of the Hamilton Depression Rating Scale and Montgomery and Åsberg Rating Scales in terms of AGE-CAT depression cases. *Int J Geriatr Psychiatry*. 2000;15:1113–9. [http://dx.doi.org/10.1002/1099-1166\(200012\)15:12<1113::AID-GP5253>3.0.CO;2-Y](http://dx.doi.org/10.1002/1099-1166(200012)15:12<1113::AID-GP5253>3.0.CO;2-Y).
42. Mukamal KJ, Rimm EB, Kawachi I, O'Reilly EJ, Calle EE, Miller M. Body mass index and risk of suicide among one million US adults. *Epidemiology*. 2010;21:82–6. <http://dx.doi.org/10.1097/EDE.0b013e3181c1fa2d>.
43. Wang YP, Gorenstein C. Assessment of depression in medical patients: a systematic review of the utility of the Beck Depression Inventory-II. *Clinics (Sao Paulo)*. 2013;68:1274–87. [http://dx.doi.org/10.6061/clinics/2013\(09\)15](http://dx.doi.org/10.6061/clinics/2013(09)15).
44. de Zwaan M. Could surgery influence psychopathology more in the long-term than evidence-based psychotherapy? Pros and cons of bariatric surgery in the treatment of obesity. *Verhaltenstherapie*. 2012;22:199–203. <http://dx.doi.org/10.1159/000341543>.

Submit your next manuscript to BioMed Central and we will help you at every step:

- We accept pre-submission inquiries
- Our selector tool helps you to find the most relevant journal
- We provide round the clock customer support
- Convenient online submission
- Thorough peer review
- Inclusion in PubMed and all major indexing services
- Maximum visibility for your research

Submit your manuscript at
www.biomedcentral.com/submit

C. Paiva-Medeiros PF, **Duarte-Guerra LS**, Santo MA, Lotufo-Neto F, Wang YP. Psychometric Properties of the Montgomery-Åsberg Depression Rating Scale in Severely Obese Patients. Span J Psychol. 2015 Sep 14;18:E69. doi: 10.1017/sjp.2015.072.

Permission for reuse by Spanish Journal of
Psychology from Cambridge University Press and
Copyright Clearance Center.

Psychometric Properties of the Montgomery-Åsberg Depression Rating Scale in Severely Obese Patients

Paula Francielle Paiva-Medeiros, Leorides Severo Duarte-Guerra, Marco Aurélio Santo, Francisco Lotufo-Neto and Yuan-Pang Wang

Universidade de São Paulo (Brazil)

Abstract. Obesity is a chronic condition worldwide and has frequent association with major depression. The Montgomery-Åsberg Depression Rating Scale (MADRS) was applied to obese patients in order to detect briefly and systematically depressive symptoms. The objectives were: to estimate the reliability of the MADRS and to investigate the criterion validity of MADRS. The best cut-off point to detect depressive symptoms was determined in comparison with the Structured Clinical Interview for DSM-IV Axis I Diagnosis (SCID-I). The sample was recruited consecutively from the waiting list of a bariatric surgery service of the university clinic. Trained clinical psychologists applied the assessment instruments. The final sample was comprised of 374 class III obese adults (women 79.9 %, mean age 43.3 years [*SD* 11.6], mean body mass index 47.0 kg/m² [*SD* 7.1]). The mean total score of the MADRS was 7.73 (*SD* 11.33) for the total sample, with a Cronbach's alpha coefficient of .93. Women presented higher mean score than men (8.08 versus 6.33; $p = .23$). The best cut-off point was 13/14 in accordance with the Receiver Operating Characteristics (ROC) curve analysis, yielding a sensitivity of .81 and specificity of .85. The overall ability to discriminate depression according to area under the curve was .87. The results showed that the MADRS is a reliable and valid scale to detect depressive symptoms among patients seeking treatment in preoperative period, displaying adequate psychometric properties.

Received 2 February 2015; Revised 2 April 2015; Accepted 12 May 2015

Keywords: depression, obesity, bariatric surgery, Montgomery-Åsberg Depression Rating Scale.

Obesity is a chronic and non-communicable condition that involves the accumulation of adipose tissue in compromising level to the physical health of individuals. According to the World Health Organization (2015), more than 1.9 billion adults, 18 years and older, were overweight in 2014, of these over 600 million were obese. The World Health Organization considers obesity a major public health problem, launching campaigns to control and prevent its increase, as well as far-reaching measures to combat its harmful consequences.

Although obesity is a major public health concern in developed countries, this scenario has expanded in recent decades. Developing countries also suffer from the rising epidemic of this chronic disease, being a foremost concern for health officials that take broad measures to stop its accelerated growth. For example, it is predicted in emerging economies like Brazil that the general population will present more non-communicable diseases, being ranked as the fifth country in the world with more obesity-associated burden in 2025 (Damaso, 2003). Recent data of 2012 indicate that 50.8% of Brazilian adults are overweight, with an overall share of 17.5% obesity

(Ministério da Saúde do Brasil, 2013). In comparison with previous survey (Ministério da Saúde do Brasil, 2007), there was an increase of almost 20% of overweight for adults and an additional 50% of respondents were considered in the level of obesity during the period.

In addition to medical problems such as cardiovascular and metabolic diseases, psychological and social consequences of obesity are relevant: with frequent emotional problems, low self-esteem, difficulties in social interaction, segregation, professional disability and stigma. It was forecast in the study Global Burden of Disease (Murray & Lopez, 1996) that major depression would be one of the disease with the highest burden to the world population in the year 2020, just behind cardiovascular diseases. The burden among obese individuals is twofold: major depressive disorder is associated frequently with cardiovascular and metabolic diseases of overweight. These problems become even more serious when obese individuals fail to adhere to a healthy lifestyle, being subjected to restrictive diets, weight-loss drugs and surgical procedures to control or reduce excessive weight.

Epidemiological studies in population samples indicate that approximately one-sixth of the population will present at least one depressive episode in lifetime (Bromet et al., 2011). Furthermore, community studies have documented the co-occurrence of obesity and depression: the likelihood of major depression among

Correspondence concerning this article should be addressed to Yuan-Pang Wang, Universidade de São Paulo, Medical School, Rua Dr. Ovídio Pires de Campos, 785. 05403-010, São Paulo (Brazil). Phone/Fax: +55-1126616976

obese individual is almost five times higher when compared with the population of body mass index (BMI) in the normal range (Onyike, Crum, Lee, Lyketsos, & Eaton, 2003; Scott, McGee, Wells, & Oakley-Browne, 2008). Studies conducted with clinical samples of morbid obesity (BMI > 40 kg/m²) show that depressive disorder is one of the most common psychiatric comorbidities, both in the pre- and the post-surgical period (Alciati, Gesuele, Rizzi, Sarzi-Puttini, & Foschi, 2011; Duarte-Guerra, Coelho, Santo, & Wang, 2015; Mühlhans, Horbach, & de Zwaan, 2009).

To the extent that depressive disorder is a frequent psychiatric disorder in obese patients, the existence of a screening instrument for detecting depressive symptoms quickly may allow their use on a large scale, facilitating early referral to appropriate treatment. For the sake of comparability and reproducibility in different populations and clinical settings, psychometric studies should be conducted to verify the reliability and validity of the instrument to measure the underlying construct of depressive symptoms in the target population, in accordance with international criteria. In operational criteria of the DSM-IV-TR (American Psychiatric Association, 2000), a major depressive episode is defined by depressive mood and/or loss of pleasure or interest in normally enjoyable activities for a minimum period of two weeks. Furthermore, the individual must meet four accessory symptoms including: sleep disturbances, appetite and/or energy changes, guilt feelings, and suicidal ideation, among other symptoms.

The research objectives were: (a) to describe the psychometric performance of the Montgomery-Åsberg Rating Scale (MADRS) to identify depressive symptoms in obese patients; (b) to estimate the reliability of MADRS; and (c) to investigate the criterion validity of the MADRS, by estimating the best cut-off point for detecting major depressive episode in comparison to international diagnostic criteria.

Methods

Sampling

The sample was recruited consecutively from the waiting list of obese patients who were undergoing bariatric surgery in the outpatient unit of the Clinics Hospital of the University of São Paulo Medical School. This service is the largest bariatric center of Brazil and Latin America, where around 200 operations are performed annually. The multidisciplinary team of treatment consists of surgeon, endocrinologist, psychologist, nurse and dietitian. The preferred surgical procedure in this gastroplastic service is the technique of Roux-en-Y.

Patients admitted to the bariatric surgery program must meet the following criteria: (a) class III obesity (BMI ≥ 40 kg/m²) or a BMI ≥ 35 kg/m² with severe

medical comorbidities; (b) be aged 18 years or more; and (c) be able to understand the risks and benefits of bariatric surgery. Eligible patients are included in a waiting list, which is sorted according to the patient's date of admission and clinical severity. Preoperative evaluations include lab workup, medical assessment, nutritional and psychological monitoring. Severe mental disorders such as psychosis and intellectual reduction are additional conditions that contraindicate bariatric surgery. Supplementary exclusion criteria of this validation study were: patients with language difficulties and previous gastroplastic surgery.

The administrative office of the bariatric clinic provided a list of 500 patients, whose names were released sequentially to the researchers in blocks of 100. The first contact with participants was conducted by telephone. The research assistants explained to patients the research objectives and invited them to set an appointment for detailed interview. Among the contacted patients, 63 individuals refused to participate during the telephone contact. Among the contacted patients who agreed to participate, 63 patients were non-eligible: 37 reported difficulty with mobility due to overweight or geographical distance and 26 were excluded from the final sample after assessment at the clinic. The reasons for exclusion were: severe psychiatric illness (one psychosis and one intellectual disability), previous bariatric surgery (five) and inability to complete the interviews (19). The final sample consisted of 374 individuals, with a participation rate of 74.8%. The interviews took place between November 2010 and March 2012 at the outpatient unit and patients were face-to-face interviewed in a single meeting. Independent interviewers, who were blind to participants' SCID-I psychiatric diagnosis, applied the MADRS. The duration of the interviews ranged from 60 to 90 minutes for the SCID-I and ranged from 10 to 40 minutes for the MADRS.

Instruments

Montgomery-Åsberg Depression Rating Scale - MADRS (Montgomery & Åsberg, 1979). This scale consists of 10 items covering mood and vegetative domains of depression and the clinical interviewer should score the intensity of depressive symptoms: between 0–6 for each item evaluated, with the possible total scores ranging between 0 and 60. The total score allows classifying the patients in following levels of severity of depression: normal or absent 0–6; mild 7–19; moderate 20–34; and severe 35–60 (Herrmann, Black, Lawrence, Szekely, & Szalai, 1998). This tool was validated in Brazilian-Portuguese language for psychiatric patients (Dratcu, Costa Ribeiro, & Calil, 1987). The present study used an interview to anchor the scores, the Structured Interview Guide for Montgomery-Åsberg Depression

Rating Scale - SIGMA (Williams & Kobak, 2008). The interviewers calibrated the MADRS' score in two meetings, with discussion of the scoring system and role-playing of the scale administration.

Structured Clinical Interview for DSM-IV Axis I - SCID-I (First, Spitzer, Gibbon, & Williams, 2002). This semi-structured interview is widely adopted as the gold standard for diagnosis of most mental disorders categories listed in the classification of the DSM-IV (American Psychiatric Association, 2000). After screening for the presence of psychopathology, the interviewer should investigate whether respondents meet the criteria for affective disorders (section A, B), psychotic disorders (C, D), substance use disorders (E), disorders of anxiety (F), somatoform disorders (G), eating disorders (H) and adjustment disorders (I). Appropriate evidence of reliability and validity has been reported in several samples of patients (Del-Ben, Rodrigues, & Zuardi, 1996). We used the patient version of SCID-I, which allow recording disorders for both current and lifetime period. The sections of psychotic disorders and somatoform disorders were not assessed to shorten the time of application.

Six clinical psychologists with previous experience in obesity and bariatric surgery were trained in 3-day standard course of SCID-I, followed by a 60 hours of calibration practice. Random pairs of researchers assessed the first 15 patients, in order to estimate the between-rater agreement. The kappa coefficient for lifetime psychiatric disorders was $k = .81$.

Statistical analysis

First, descriptive analysis with a mean (M) and standard deviation (SD) of the MADRS score was performed for the total sample and by gender. The reliability of the MADRS was calculated using the Cronbach's alpha coefficient of internal consistency.

Following, the signal detection analysis determined the best cut-off point, adopting the diagnosis of DSM-IV major depressive disorder as the gold standard. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of all possible thresholds were calculated. The best cut-off point was determined as the threshold with the best tradeoff between sensitivity and specificity. The Receiver Operating Characteristic (ROC) curve was built from rates of sensitivity and false positive data ($1 - \text{specificity}$), which also allowed us to estimate the area under the ROC curve (AUC) for estimating the accuracy for detecting performance MADRS depressive symptoms.

All analyses were performed using SPSS software, version 18.0 (IBM Inc., 2009); the level of statistical significance was set at 0.05, for two-tailed tests.

Ethical aspects

The Ethics Committee of the University of São Paulo Medical School approved the study. Participants were assured that information provided for research would not influence their schedule or eligibility for surgery. All participants have signed an informed consent.

Results

For the final sample, 374 patients participated in this study, being 79.9% women ($n = 299$) and 20.1% men ($n = 75$), with mean BMI 47.0 kg/m^2 ($SD = 7.1$), and mean age 43.3 years ($SD = 11.6$). The Cronbach's alpha coefficient of internal consistency of the MADRS was .93, showing substantial consistency of the MADRS and the ability of their items to assess homogeneously the target construct.

Table 1 shows the endorsement rate of depressive symptoms in obese patients in MADRS, in terms of mean (M) and standard deviation (SD). For the total sample, the mean total score placed the group in the severity level of "mild" depression ($M_t = 7.72$; $SD = 11.33$). Regarding individual items, most of participants scored around 1.0 or lower. The most frequent endorsed symptoms were "apparent sadness", followed by "reduction of sleep", "reported sadness" and "inner tension". Moreover, the less frequent symptoms were "suicide" and "decreased appetite". Although women have endorsed more symptoms and displayed higher mean total score than men ($M_w = 8.08$ versus $M_m = 6.33$; $p = .23$), this difference was not statistically significant after the analysis of variance (ANOVA) to compare the total and item scores. These results indicated that the MADRS can detect cases of mild depression by the total scores strategy. While women are more easily classified above the threshold of depression > 7 , men are below the threshold.

Among the participants, 27.5% ($n = 103$) met the criteria of major depressive episode according to the DSM-IV. The contingency table 2×2 was constructed for all possible cut-offs for MADRS, taking as comparison the gold standard SCID-I. These tables allowed estimating the number of true positive and negative cases, and the false positive and false negative cases for each cut-off point. The contingency tables allowed determining following indicators: sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Table 2 shows the range of cut-off points with acceptable or appropriate performance and the best cut-off point was set as 13/14. This threshold was determined by the tradeoff between the maximum performance of sensitivity and specificity. For this cut-off, the sensitivity was 85% and specificity was 81%. The resulting PPV was 70% and the NPV 91%, showing that this cut-off point is capable of detecting

Table 1. Mean (M) and standard deviation (SD) of the Montgomery-Åsberg Depression Rating Scale for obese patients, total sample and by gender

Item	Total N = 374		Women n = 299		Men n = 75	
	M	SD	M	SD	M	SD
Apparent sadness	1.10	1.70	1.15	1.74	0.93	1.55
Reported sadness	0.99	1.72	1.06	1.78	0.73	1.43
Inner tension	0.94	1.47	1.00	1.51	0.72	1.31
Reduced sleep	1.00	1.63	1.00	1.62	1.03	1.66
Reduced appetite	0.48	1.08	0.53	1.14	0.27	0.79
Concentration difficulties	0.74	1.39	0.79	1.44	0.52	1.18
Lassitude	0.76	1.38	0.77	1.40	0.72	1.34
Inability to feel	0.76	1.45	0.79	1.45	0.67	1.44
Pessimistic thoughts	0.63	1.35	0.64	1.36	0.56	1.32
Suicidal thoughts	0.33	0.99	0.36	1.02	0.19	0.87
Total	7.73	11.33	8.08	11.60	6.33	10.14

Table 2. Sensitivity, specificity, positive and negative predictive values and best cut-off point for score of the Montgomery-Åsberg Depression Rating Scale among obese patients (n = 374)

Cut-off	5/6	6/7	7/8	8/9	9/10	10/11	11/12	12/13	13/14*	14/15	15/16	16/17	17/18	18/19
Sensitivity	.92	.92	.92	.90	.87	.85	.85	.85	.85	.77	.69	.65	.65	.58
Specificity	.64	.66	.69	.70	.74	.76	.77	.81	.81	.83	.84	.86	.86	.89
Positive predictive value	.52	.56	.56	.57	.59	.60	.62	.69	.70	.72	.72	.75	.75	.80
Negative predictive value	.95	.95	.95	.94	.93	.92	.92	.91	.91	.86	.82	.79	.79	.74

*Tradeoff between sensitivity and specificity.

around 90% of cases of depression in comparison with the gold standard SCID-I.

Among the 103 patients classified as depressed by structured interview SCID-I, the new 13/14 MADRS threshold failed to detect 16 subjects. Using this threshold, patients who rated below this point was considered non-depressed and those that scored above were considered depressed (Table 3), with an average score significantly higher than non-depressed obese ($M_d = 24.96$ versus $M_{nd} = 3.35$, $p < .0001$). According to the new threshold estimated by the gold standard, the severity level of depression detected among obese patients would be classified as of "moderate" intensity.

Following, the sensitivity and proportion of false positive (1 - specificity) were used to build the ROC curve. These indicators were plotted in comparison with the category of DSM-IV depressive disorders as yielded by SCID-I (Figure 1). The calculation of the area under the ROC curve (AUC) showed that the accuracy or performance of the MADRS was satisfactory (AUC = .87; CI95% .82 - .92), as the scale could properly identify the vast majority of cases of depression.

Discussion

Despite conspicuous literature linking obesity and depressive disorders, there are not psychometric studies investigating the applicability of MADRS in severely obese patients. The present study demonstrated that the MADRS presents suitable psychometric characteristics, with good internal consistency and appropriate validity to identify depressive disorders among pre-operative obese patients who were waiting for surgical procedures. The scale has shown to be able to detect approximately nearly 90% of cases of depression with the final threshold of 13/14. The mean score of 7.7 marginally detected possible cases of "mild depression", but the subjects who scored above the best cut-off point had a severity level that was compatible with "moderate depression". This differential performance qualifies MADRS as a versatile and efficient tool to screen quickly and to refer the case of obese patients with depression to treatment in various settings, for example, in its pre-surgical period. Its psychometric performance was considered robust, with good sensitivity and specificity, and there was no statistically significant influence of gender. The psychometric properties of

Table 3. Mean (*M*) and standard deviation (*SD*) of the Montgomery-Åsberg Depression Rating Scale for non-depressed and depressed obese patients, in accordance with the 13/14 threshold

MADRS	<i>N</i>	<i>M</i>	<i>SD</i>	%
Non-depressed	285	3.35	3.53	76.2
Depressed	89	24.96*	10.48	23.8
Total	374	7.73	11.33	100.0

*ANOVA $F = 8.95$; $p < .0001$.

the scale are also strengthened by its positive acceptance by the user, being a cost-effective tool for rapid implementation and easy to understand.

In general, satisfactory reliability can be confirmed by the majority of similar studies investigating MADRS, with the reported Cronbach's alpha coefficient close to .80 (Bunevicius et al., 2012; Muller-Thomsen, Arlt, Mann, Mass, & Ganzeret 2005; Mundt et al., 2006;). Since the reliability assurance is a premise to investigate the validity of the construct being assessed, it is safe to assume that the favorable psychometric performance can be partly attributed to the consistency of the MADRS, indicating homogeneity of the items that make up the scale to measure the same target construct.

Introduced in 1979, the MADRS scale is widely used in several clinical populations (Bunevicius et al., 2012; Leentjens, Verhey, Lousberg, Spitsbergen, & Wilmink, 2000; Magnil, Gunnarsson & Bjorkelund, 2011; Portugal et al., 2012; Sarro, 2004) being applied in many follow-up studies and clinical trials (Zimmerman, Chelminski, & Posternak, 2004). Nevertheless, researchers still inquire about which cut-off should be adopted for their sample. The cut-off point may vary depending on the

characteristics of the disease and respondents, the objective and the methodology of the investigation.

Taking into account the characteristics of the population under investigation, the score of some MADRS items should be interpreted with caution, wherein their improper use can alter the performance of the scale for the planned purpose – i.e., how large is the tolerable number of cases of false positives or false negatives. Specifically, the low score of the symptom endorsement of “decreased appetite” in obese patients indicates that this symptom has little utility in assessing people who present overeating behavior, even in depressed state. This item can reduce the total score and decrease the identification of active cases of depression among obese. Similarly, the symptom of “suicidal ideation” was observed so infrequently among men, which can cause differential between-sex performance when applying the MADRS, although ANOVA results showed that there is no difference between sex for total mean score. Some depressed men were unable to be detected as depressed in agreed-upon threshold and different cut-off points may be necessary for each sex. It is suggested that future studies with MADRS incorporate a thorough analysis in relation to differential item functioning by Item Response Theory and review the need to include all items in specific populations.

The mean total scores in our study were able to identify cases of “mild” depression, but would detect only 56% of true positive cases, especially obese women in the study. However, examining the psychometric parameters of MADRS for the region between 5–9, we observe that the scale has detected cases of depression with substantial sensitivity, identifying more than 90% of probable cases. Further, the specificity of approximately 70% along with lower PPV can be of little help to identify those active cases. Notwithstanding, the sensitivity of

Figure 1. Receiver Operating Characteristic Curve of the Montgomery-Åsberg Depression Rating Scale.

the MADRS has reduced slightly in the region between 10 and 14, but still present acceptable performance that was accompanied by considerable improvement of its specificity. In the cut-off point of 13/14, we achieved an increase in PPV without substantial loss in NPV. These results indicate that the threshold of > 7 proposed by Herrmann et al. (1998), may be too sensitive and it is recommended for population screening studies of probable cases of "mild" depression. If a researcher needs to ensure the specificity of detecting cases of depression, the adopted threshold should be higher. While the threshold 6/7 identified cases of "mild" depression, we observed that cases of depressed obese were classified at a level of "moderate" depression as we raise the threshold to 13/14. Therefore, careful psychometric studies are essential to help the researcher to establish the best cut-off point according to their research objectives.

In comparison to studies that investigated the criterion validity of the MADRS (Bunevicius et al., 2012; Leentjens et al., 2000; Magnil et al., 2011; Mottram, Wilson, & Copeland, 2000; Muller-Thomsen et al., 2005; Portugal et al., 2012; Riedel et al., 2010; Reijnders, Lousberg, & Leentjens, 2010), three studies reported the best cut-off of 13/14 (Magnil et al., 2011; Muller-Thomsen et al., 2005; Reijnders et al., 2010). The thresholds ranged from 6 to 21, and the study Riedel et al. (2010) reported the cut-off point of 6/7 for bipolar patients and Mottram et al., (2000) of 20/21 for geriatric sample. Interestingly, the results of the obese population were similar to validation data from patients with cognitive impairments such as Alzheimer's disease and Parkinson's disease (Muller-Thomsen et al., 2005; Reijnders et al., 2010). In a psychometric study with elderly patients (Yoon et al., 2012), the authors suggested an association between high BMI and cognitive decline. More studies are needed to confirm this potential association.

Some characteristics of medical conditions can hamper the implementation of definite psychometric instruments. The easy applicability of a short scale as MADRS has the advantage of serving as a standardized instrument for use in various clinical settings (Bunevicius et al., 2012; Leentjens et al., 2000; Magnil et al., 2011; Portugal et al., 2012; Sarro et al., 2004) saving the time of busy professionals in conducting lengthy interviews. Although several studies validating psychometric scales have adopted the MADRS as the comparison tool (Mottram et al., 2000; Portugal et al., 2012), there is limited evidence on psychometric performance of the MADRS. The format of the observer scale of MADRS has the advantage of allowing comprehensive comparisons of depressive symptoms in different clinical populations, such as individuals with cognitive impairments, with limited understanding, clinical

diseases that obstruct the use of self-administration scales. The usefulness of a validated scale to assess depressive symptoms in clinical samples is unquestionable when one in four patients present clinical depression (Hedman et al., 2014; Muller-Thomsen et al., 2005; Mundt et al., 2006; Portugal et al., 2012). In our study of diagnostic evaluation of bariatric obese patients (Duarte-Guerra et al., 2015), one in five participants met the diagnostic criteria for a current depressive episode according to DSM-IV system, confirming the relevance of psychiatric disorders among medical patients.

Most studies have indicated that the MADRS can detect approximately 90% of cases of depression, which ranged from 80% to 96% (Kang et al., 2013; Mottram et al., 2000; Portugal et al., 2012; Reijnders et al., 2010; Riedel et al., 2010). However, some methodological differences may explain the different rates of depressive symptoms observed in various populations. For example, the method of data collection might have affected their performance: while some studies have completed telephone interview (Mundt et al., 2006), other studies have taken personal interviews. The advantages of each method of collection over self-report inventories should not be stated, since formal comparisons were not tested. Anyway, the frequency of depressive symptoms may change in accordance to the methodology of data collection.

Some obese population characteristics should be taken into consideration in the interpretation of psychometric scales. Besides the physical difficulties to undergo extensive interviews due to overweight, bariatric patients tend to mask their emotional and physical symptoms (de Zwaan, 2012), fearing that an unfavorable diagnosis could disturb the schedule of their surgical procedure, generating many cases of false negatives with underestimate of psychiatric disorders. Many patients may have not disclosed problems being afraid of negative results of the assessment, which might lead to the disapproval or delay of surgery. Conversely, exaggerating their symptoms could serve to by-pass their ranking in the waiting list, resulting in cases of false positives. Thus, a structured observer scale as MADRS, conducted by an experienced interviewer reduces the possibility of distortion of symptom detection. Probably, this type of instrument is superior over self-report scales (Wang & Gorenstein, 2013). In a recent study that applied the Beck Depression-II in obese patients (Hayden Brown, Brennan, & O'Brien, 2012), they observed a significant proportion of false positive cases and low rate of self-reported depressive symptoms. Some clinical samples with special requirements may be adapted to meet the specific needs of each population - in our case, class III obese patients waiting for surgery. Thus, an observer scale with proper demonstration of criterion validity as the

MADRS is recommended for use among obese people in the pre-surgical period.

Some limitations of this study should be considered before generalizing the data of this investigation for obese population. All participants in the sample were recruited from the same university hospital, raising doubts about the representativeness of the profile of obese participants who agreed to participate in the interview. Although the evaluations are carried out independently of the preoperative screening and surgical approval process, it is possible that patients have omitted, underestimated or exaggerated their symptoms, fearing interference in the schedule of surgery, distorting the actual frequency of psychiatric symptoms - known as "impression management" in the literature (de Zwaan, 2012). Possibly, clinical comorbidities associated with obesity and the medication used by this population may confuse the symptoms reported, for example, "fatigue" is often reported by physically compromised patients and can easily be interpreted as a depressive symptom. Finally, the cross-sectional design of this study limits the scope of the results, is desirable following-up patients in both the pre and post-surgical phase with longitudinal design to strengthen the information on the stability and sensitivity to change of MADRS in obese population.

Our study evaluated the psychometric performance of the MADRS scale in pre-surgical patients, adopting a semi-structured interview SCID-I as the gold standard. Our findings showed that the MADRS scale is an effective tool in bariatric pre-operative evaluation, with accurate and robust psychometric properties, in relation to both reliability and validity. The systematic detection of depressive psychopathology with structured and validated instruments (Mechanick et al., 2013) during the pre-surgical evaluation can contribute to a better prognosis in the postoperative period. The recommendation of incorporating effective evaluation of individuals with overweight and obesity in clinical practice guidelines can improve the surgical indication of obese patients and reduce their disease burden during the follow-up period.

References

- Alciati A., Gesuele F., Rizzi A., Sarzi-Puttini P., & Foschi D. (2011). Childhood parental loss and bipolar spectrum in obese bariatric surgery candidates. *International Journal of Psychiatry Medicine*, 41, 155–171. <http://dx.doi.org/10.2190/PM.41.2.e>
- American Psychiatric Association. (2000). *Diagnostic And Statistical Manual Of Mental Disorders DSM-IV-TR Fourth Edition* (Text Revision). Washington DC: American Psychiatric Press.
- Bromet E., Andrade L. H., Hwang I., Sampson N. A., Alonso J., de Girolamo G., ... Kessler R. C. (2011). Cross-national epidemiology of DSM-IV major depressive episode. *BioMed Central Medicine*, 9, 90. <http://dx.doi.org/10.1186/1741-7015-9-90>
- Bunevicius A., Staniute M., Brozaitiene J., Pommer A. M., Pop V. J., Montgomery S. A., & Bunevicius R. (2012). Evaluation of depressive symptoms in patients with coronary artery disease using the Montgomery Åsberg Depression Rating Scale. *International Clinical Psychopharmacology*, 27, 249–255. <http://dx.doi.org/10.1097/YIC.0b013e328357670d>
- Damaso A. (2003). *Etiologia da obesidade* [The etiology of obesity]. Rio de Janeiro, Brazil: Medsi.
- de Zwaan M. (2012). Could Surgery influence Psychopathology more in the long-term than evidence-based psychotherapy? Pros and cons of bariatric surgery in the treatment of obesity. *Verhaltenstherapie*, 22, 199–203. <http://dx.doi.org/10.1159/000341543>
- Del-Ben C. M., Rodrigues C. R., & Zuardi A. W. (1996). Reliability of the Portuguese version of the structured clinical interview for DSM-III-R (SCID) in a Brazilian sample of psychiatric outpatients. *Brazilian Journal of Medical and Biological Research*, 29, 1675–1682.
- Dratcu L., da Costa Ribeiro L., & Calil H. M. (1987). Depression assessment in Brazil. The first application of the Montgomery-Åsberg Depression Rating Scale. *British Journal of Psychiatry*, 150, 797–800.
- Duarte-Guerra L. S., Coelho B. M., Santo M. A., & Wang Y. P. (2015). Psychiatric disorders among obese patients seeking bariatric surgery: Results of structured clinical interviews. *Obesity Surgery*, 25, 830–837. <http://dx.doi.org/10.1007/s11695-014-1464-y>
- First M. B., Spitzer R. L., Gibbon M., & Williams J. B. W. (2002). *Structured clinical interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition*. New York, NY: Biometrics Research, New York State Psychiatric Institute.
- Hayden M. J., Brown W. A., Brennan L., & O'Brien P. E. (2012). Validity of the Beck Depression Inventory as a screening tool for a clinical mood disorder in bariatric surgery candidates. *Obesity Surgery*, 22, 1666–1675. <http://dx.doi.org/10.1007/s11695-012-0682-4>
- Hedman E., Ljotsson B., Kaldö V., Hesser H., El Alaoui S., Kraepelien, ... Lindefors N. (2014). Effectiveness of Internet-based cognitive behavior therapy for depression in routine psychiatric care. *Journal of Affective Disorders*, 155, 49–58. <http://dx.doi.org/10.1016/j.jad.2013.10.023>
- Herrmann N., Black S. E., Lawrence J., Szekely C., & Szalai J. P. (1998). The Sunnybrook Stroke Study: A prospective study of depressive symptoms and functional outcome. *Stroke*, 29, 618–624. <http://dx.doi.org/10.1161/01.STR.29.3.618>
- IBM Inc. (2009). PASW Statistics for Windows (Version 18.0). Chicago, IL: SPSS Inc.
- Kang H. J., Stewart R., Kim J. M., Jang J. E., Kim S. Y., Bae K. Y., ... Yoon J. S. (2013). Comparative validity of depression assessment scales for screening poststroke depression. *Journal of Affective Disorders*, 147, 186–191. <http://dx.doi.org/10.1016/j.jad.2012.10.035>
- Leentjens A. F., Verhey F. R., Lousberg R., Spitsbergen H., & Wilmink F. W. (2000). The validity of the Hamilton and Montgomery-Åsberg depression rating scales as screening

- and diagnostic tools for depression in Parkinson's disease. *International Journal of Geriatric Psychiatry*, 15, 644–649.
- Magnil M., Gunnarsson R., & Bjorkelund C.** (2011). Using patient-centred consultation when screening for depression in elderly patients: A comparative pilot study. *Scandinavian Journal of Primary Health Care*, 29(1), 51–56. <http://dx.doi.org/10.3109/02813432.2011.554011>
- Mechanick J. I., Youdim A., Jones D. B., Garvey W. T., Hurley D. L., McMahon M. M., ... Brethauer S.** (2013). Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient—2013 update: Cosponsored by american association of clinical endocrinologists, the obesity society, and american society for metabolic & bariatric surgery. *Obesity*, 21(S1), S1–S27. <http://dx.doi.org/10.1002/oby.20461>
- Ministério da Saúde do Brasil.** (2007). *Vigitel Brasil 2006: Vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico*. [Vigitel Brasil 2006: The surveillance of risk and protective factors for chronic diseases by telephone survey]. Brasília, Brazil: Ministério da Saúde.
- Ministério da Saúde do Brasil.** (2013). *Vigitel Brasil 2012: Vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico* [Vigitel Brasil 2012: The surveillance of risk and protective factors for chronic diseases by telephone survey]. Brasília, Brazil: Ministério da Saúde.
- Montgomery S. A., & Asberg M.** (1979). A new depression scale designed to be sensitive to change. *British Journal of Psychiatry*, 134, 382–389. <http://dx.doi.org/10.1192/bjp.134.4.382>
- Mottram P., Wilson K., & Copeland J.** (2000). Validation of the Hamilton Depression Rating Scale and Montgomery and Asberg Rating Scales in terms of AGE-CAT depression cases. *International Journal of Geriatric Psychiatry*, 15, 1113–1119. [http://dx.doi.org/10.1002/1099-1166\(200012\)15:12%3C1113::AID-GPS253%3E3.0.CO;2-Y](http://dx.doi.org/10.1002/1099-1166(200012)15:12%3C1113::AID-GPS253%3E3.0.CO;2-Y)
- Muller-Thomsen T., Arlt S., Mann U., Mass R., & Ganzer S.** (2005). Detecting depression in Alzheimer's disease: Evaluation of four different scales. *Archives of Clinical Neuropsychology*, 20, 271–276. <http://dx.doi.org/10.1016/j.acn.2004.03.010>
- Mundt J. C., Katzelnick D. J., Kennedy S. H., Eisfeld B. S., Bouffard B. B., & Greist J. H.** (2006). Validation of an IVRS version of the MADRS. *Journal of Psychiatry Research*, 40, 243–246. <http://dx.doi.org/10.1016/j.jpsychires.2005.05.002>
- Murray C. J. L., & Lopez A. D.** (1996). *The global burden of disease: A comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020* (Vol. 1). Cambridge, MA: Harvard University Press.
- Mühlhans B., Horbach T., & de Zwaan M.** (2009). Psychiatric disorders in bariatric surgery candidates: A review of the literature and results of a German prebariatric surgery sample. *General Hospital Psychiatry*, 31, 414–421. <http://dx.doi.org/10.1016/j.genhosppsych.2009.05.004>
- Onyike C. U., Crum R. M., Lee H. B., Lyketos C. G., & Eaton W. W.** (2003). Is obesity associated with major depression? Results from the Third National Health and Nutrition Examination Survey. *American Journal of Epidemiology*, 158, 1139–1147. <http://dx.doi.org/10.1093/aje/kwg275>
- Portugal G., Coutinho E. S., Almeida C., Barca M. L., Knapskog A. B., Engedal K., & Laks J.** (2012). Validation of Montgomery-Asberg Rating Scale and Cornell Scale for Depression in Dementia in Brazilian elderly patients. *International Psychogeriatrics*, 24, 1291–1298. <http://dx.doi.org/10.1017/s1041610211002250>
- Reijnders J. S. A. M., Lousberg R., & Leentjens A. F. G.** (2010). Assessment of depression in Parkinson's disease: The contribution of somatic symptoms to the clinimetric performance of the Hamilton and Montgomery-Asberg rating scales. *Journal of Psychosomatic Research*, 68, 561–565. <http://dx.doi.org/10.1016/j.jpsychores.2009.10.006>
- Riedel M., Moller H. J., Obermeier M., Schennach-Wolff R., Bauer M., Adli M., ... Seemuller F.** (2010). Response and remission criteria in major depression—a validation of current practice. *Journal of Psychiatric Research*, 44, 1063–1068. <http://dx.doi.org/10.1016/j.jpsychires.2010.03.006>
- Sarro S., Duenas R. M., Ramirez N., Arranz B., Martinez R., Sanchez J. M., ... San L.** (2004). Cross-cultural adaptation and validation of the Spanish version of the Calgary Depression Scale for Schizophrenia. *Schizophrenia Research*, 68, 349–356. [http://dx.doi.org/10.1016/s0920-9964\(02\)00490-5](http://dx.doi.org/10.1016/s0920-9964(02)00490-5)
- Scott K. M., McGee M. A., Wells J. E., & Oakley Browne M. A.** (2008). Obesity and mental disorders in the adult general population. *Journal of Psychosomatic Research*, 64(1), 97–105. <http://dx.doi.org/10.1016/j.jpsychores.2007.09.006>
- Wang Y. P., & Gorenstein C.** (2013). Assessment of depression in medical patients: A systematic review of the utility of the Beck Depression Inventory-II. *Clinics (Sao Paulo)*, 68, 1274–1287. [http://dx.doi.org/10.6061/clinics/2013\(09\)15](http://dx.doi.org/10.6061/clinics/2013(09)15)
- Williams J. B. W., & Kobak K. A.** (2008). Development and reliability of a structured interview guide for the Montgomery Asberg Depression Rating Scale (SIGMA). *British Journal of Psychiatry*, 192(1), 52–58. <http://dx.doi.org/10.1192/bjp.bp.106.032532>
- World Health Organization WHO** (2015). *Obesity and overweight*. Media Center, Fact Sheets. Genève, Switzerland: Author. Retrieved from <http://www.who.int/mediacentre/factsheets/fs311/en/>
- Yoon D. H., Choi S. H., Yu J. H., Ha J. H., Ryu S. H., & Park D. H.** (2012). The relationship between visceral adiposity and cognitive performance in older adults. *Age & Ageing*, 41, 456–461. <http://dx.doi.org/10.1093/ageing/afs018>
- Zimmerman M., Chelminski I., & Posternak M. A.** (2004). Review of studies of the Montgomery-Asberg Depression Rating Scale in controls: Implications for the definition of remission in treatment studies of depression. *International Clinical Psychopharmacology*, 19(1), 1–7. <http://dx.doi.org/10.1097/00004850-200401000-00001>

D. Lasagni V, Palma R, Rios B, Vázquez-Velásques V, **Duarte-Guerra LS**, Malischesqui Paegle I, Graf B, Lyng V, Sanches Salvatierra M. Propuesta de guía para el tratamiento de la reganancia de peso después de cirugía bariátrica. Proposal of a guide for the treatment of weight regain afther bariatric surgery. *Bariátrica & Metabólica Ibero-Americana*. 8.2.12:2318-2322. 2018.

Free for reuse by BMI - Bariátrica & Metabólica Ibero-Americana from Journal of the Spanish Society of Metabolic and Bariatric Surgery (SECO/FUNSECO)

Artículo Original Psicología

Propuesta de guía para el tratamiento de la reganancia de peso después de cirugía bariátrica

Proposal of a guide for the treatment of weight regain after bariatric surgery

Lasagni V.(1); Palma R.(1); Ríos B(2); Vázquez-Velázquez V(3); Severo Duarte-Guerra L(4); Malischesqui Paegle I (5); Graf B (6); Lyng V(6); Sánchez Salvatierra M(7)

1Centro Quirúrgico de la Obesidad. Mendoza. Argentina, 2 Instituto de Obesidad y Síndrome Metabólico del Hospital Ángeles Pedregal. Ciudad de México. México, 3 Clínica de Obesidad y Trastornos de Conducta Alimentaria, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Ciudad de México. México, 4 Consultorio de Psicología. Santo André - São Paulo- Brasil, 5 Centro Avanzado de Gastroenterología y Cirugía de la Obesidad - Gastro Obeso Center. Brasil, 6 Centro de Atención. Solución Integral a la Obesidad y Síndrome Metabólico SIOS. Viña del Mar. Chile, 7 Centro Médico Foianini. Santa Cruz de la Sierra. Bolivia
✉ vivilasagni@hotmail.com

Resumen: Introducción: La cirugía bariátrica es efectiva para el tratamiento de la obesidad, no obstante se puede recuperar peso tras unos años de haberse efectuado este procedimiento. Esta inquietud fue abordada por un grupo de expertos en el Workshop realizado en el XI Congreso Internacional de Cirugía Bariátrica y Metabólica realizado en la ciudad de Mendoza, Argentina el 18 de Mayo de 2017. Antecedentes: Existen factores conductuales que facilitan la reganancia de peso después de la cirugía bariátrica, incluyendo la falta de adherencia al tratamiento postquirúrgico, comer impulsivamente, la disminución del bienestar y patologías psiquiátricas. **Objetivo:** Elaborar una guía de tratamiento psicológico para abordar la reganancia de peso en personas sometidas a cirugía bariátrica. **Metodología:** En el marco del congreso, psicólogos bariátricos de Argentina, Brasil, Bolivia, Chile y México, redactaron directrices sobre el manejo de la reganancia de peso en pacientes con cirugía bariátrica. **Resultados:** se elaboró una guía de actuación que pretende ser una herramienta para el tratamiento de la reganancia de peso en pacientes bariátricos. **Conclusión:** La labor del psicólogo estará dirigida a determinar los factores que han contribuido a la reganancia de peso, para reorientar el tratamiento, de modo a favorecer y mantener el descenso de peso.

Palabras clave: Cirugía bariátrica, Reganancia de peso, psicología bariátrica, obesidad.

Abstract: Introduction: Bariatric surgery is the most effective treatment for obesity, although, weight regain is possible after a few years after performing surgery. This concern was addressed by a group of experts during a workshop at the XI International Congress of Metabolic and Bariatric Surgery, in the city of Mendoza, Argentina on May 18, 2017. Background: Behavioral factors such as, lack of adherence to postsurgical treatment, impulsive eating, decreased emotional well-being and psychiatric disorders may increase the probabilities of weight regain. **Objective:** To elaborate a psychological treatment guide to address weight regain in persons who have undergone bariatric surgery. **Methodology:** Within the framework of the congress, bariatric psychologist from Argentina, Brazil, Bolivia, Chile and Mexico developed a set of guidelines to manage weight regain in bariatric surgery patients. Results: Elaboration of working guidelines aimed for the treatment of weight regain in bariatric patients after surgery. **Conclusion:** The psychologist role is to determine the contributing factors of the patient's weight regain and to redirect the treatment to promote and maintain weight loss.

Keywords: Bariatric surgery, weight regain, bariatric psychology, obesity.

Introducción

La cirugía bariátrica ha demostrado ser muy efectiva en el tratamiento de la obesidad, no obstante algunas personas pueden recuperar peso tras unos años de efectuado este procedimiento. Esta inquietud fue trabajada por un grupo de expertos en el Workshop realizado en el XI Congreso Internacional de Cirugía

Bariátrica y Metabólica realizado en la ciudad de Mendoza del 17 al 20 de mayo de 2017 en donde se pretendió elaborar una propuesta como guía para el diagnóstico y tratamiento de la reganancia de peso tras cirugía bariátrica.

A partir de una revisión bibliográfica se pudo observar en primer lugar que no existe una única definición sobre el concepto de reganancia de peso. En la tabla N°

1 se muestran las múltiples definiciones que existen, a saber

- Recuperación del 25% de peso después del peso nadir luego de dos años de realizada la cirugía.
 - Ganancia de $\geq 15\%$ de la máxima pérdida de peso inicial.
 - Cuando un paciente vuelve a tener un IMC ≥ 35 .
 - Ganancia de más de 10 kilos del peso nadir.
 - Cualquier ganancia de peso después de la remisión de DMT2.
 - Un incremento en el IMC de $5\text{kg}/\text{m}^2$ o más sobre el peso nadir.
- **Peso Nadir:** es el peso más bajo alcanzado después de la cirugía

Tabla Nº 1. Definiciones de reganancia de peso después de cirugía bariátrica.(1) Fuente: Lauti, M. Kularatna, M.

Hill, AG. Mac Cormick, AD.(2016)

En un análisis de los factores conductuales que facilitan la reganancia después de la cirugía, se encontró que el comer impulsivamente aumentaba en 5 veces la probabilidad de reganar peso, al igual que no asistir a controles periódicos. Además los individuos con malestar psicológico tenían 25 veces más posibilidad de reganar (2). En otro estudio de Odom, et al (3) se identificaron predictores conductuales en la recuperación de peso en pacientes con derivación gastroyeyunal como el aumento de comportamientos adictivos, disminución del bienestar, menor número de visitas post-operatorias de seguimiento y falta de auto-monitoreo. Otro grupo de investigadores demostró una correlación positiva entre el número de enfermedades psiquiátricas diagnosticadas después de la cirugía y el aumento de peso donde incluyeron depresión, ansiedad, ingesta compulsiva y un historial de intentos de suicidio (4).

La reganancia de peso también puede ocurrir por adaptaciones fisiológicas y anatómicas después de cierto tiempo transcurrido después de la cirugía bariátrica.

Hay varios factores que influyen en la aparición de la reganancia de peso (5);

1. Tipo de cirugía
2. Adherencia
3. Tolerancia a los alimentos (se puede reganar peso aún con intolerancias a alimentos, debido a que la ingesta puede exceder los requerimientos)
4. Opciones de alimentos y bebidas (consumo de alimentos con alta densidad calórica)
5. Prescripción energética post-quirúrgica inadecuada

6. Drivers (televisión, ingesta de alcohol, falta de sueño)
7. Desconocimiento del paciente (en ocasiones no saben que puede ocurrir la reganancia de peso)
8. Errores en la estimación de ingesta (subestiman la ingesta real en un 20 a 50 %)

En el análisis de la bibliografía efectuado se observó un escaso material en relación al tratamiento de la reganancia de peso post tratamiento quirúrgico de la obesidad por tal motivo es que se puso de manifiesto la necesidad de contribuir en la confección de este documento.

Metodología

Desde la organización del comité académico de la sección de psicología bariátrica del congreso mencionado se seleccionó un grupo de psicólogos bariátricos con experiencia en el área de diferentes países latinoamericanos a saber: Argentina, Brasil, Bolivia, Chile y México.

En una primera etapa, se elaboró un fichero de material bibliográfico respecto a la temática a investigar y se realizó una distribución de artículos científicos entre los especialistas a fin de que cada uno resaltara los datos más relevantes de artículo y elaborara una ficha bibliográfica. Posteriormente se realizó un workshop durante el desarrollo del congreso donde se llevo a cabo la discusión del material bibliográfico, se integró el material y confeccionó una guía de actuación para el tratamiento de la reganancia de peso post-cirugía bariátrica consensuada entre los expertos de área de psicología bariátrica.

Discusión

Uno de los primeros puntos a discutir fue la definición o que parámetros existen para determinar que una persona con tratamiento quirúrgico de la obesidad habría desarrollado reganancia de peso. La mayoría de los especialistas coincidieron que a la fecha no había una definición clara al respecto. Recientemente un documento de la Sociedad Brasileira de Cirugía Bariátrica y Metabólica (6) publica un documento donde se expresa que la intervención quirúrgica es segura y eficaz a largo plazo, permite controlar la enfermedad y sus comorbilidades. Aun así, se espera que un 1,3 % de las personas presenten una recidiva tardía. Clasifican a esta recidiva de la siguiente manera: a) Recidiva: Recuperación del 50% del peso perdido a largo plazo o recuperación de 20% del peso asociado al re-apareamiento de comorbilidades; b) Recidiva Controlada: Recuperación entre 20 y 50% del peso perdido en largo plazo y c) Reganancia de peso esperada: Recuperación <20% del peso perdido en largo plazo.

Posteriormente se analizaron los factores probables de reganancia peso donde se enumeraron diferentes causas extraídas de la práctica profesional. Una de las primeras causas observadas y discutidas fue el reemplazo de la ingesta de alimentos por un aumento en el consumo de alcohol. Estos coinciden con los estudios de donde constataron que el aumento de peso puede estar relacionado con comportamientos adictivos como la ingesta de alcohol (3). Otra causa observada es el retorno a conductas inapropiadas como el picoteo, la ingesta nocturna y emocional lo cual coincide con otros autores como Faria, S. L., et al (7), donde establecen que el desorden en los horarios de las comidas, la incorporación de snacks y alimentos dulces favorecen el malestar psicológico y la reganancia de peso. También se manifestó sobre factores ambientales como los relacionados a la ocupación en oficios gastronómicos que dificultan a las personas a adaptarse a nuevos hábitos. Siguiendo con el análisis de las causas de reganancia se enumeraron otras como: la falta de adherencia a los tratamientos postquirúrgicos y los controles coincidiendo con los estudios de Pataky, Z. et al, (2) la escasa o ausencia de actividad física; la falta de apoyo de la red social y/o familiar y la dificultad de adaptarse a una nueva imagen corporal en especial por el excedente de piel, lo cual se registra en las narrativas de las personas operadas quienes manifiestan hasta causarles dificultades sexuales entre otros. Cabe agregar que también merece una gran importancia resaltar que uno de los grandes ejes deberá estar centrado en una buena valoración pre-quirúrgica dado que si existen enfermedades psiquiátricas preexistentes seguramente

determinarán el fracaso de la cirugía tal cual lo manifiesta el grupo de Rutledge, T, et al (4).

Resultados

Escasos registros en relación al porcentaje de personas con tratamiento quirúrgico de la obesidad que recuperan peso. A veces por qué los equipos no poseen los mencionados registros publicados, otras por que resulta dificultoso realizar dichos registros dado que suelen abandonar los tratamientos y no vuelven a la consulta o por que vuelven después de un tiempo prolongado. Independiente al porcentaje de casos con recuperación de peso resulta necesario establecer una guía de actuación psicológica para el tratamiento de la reganancia de peso post cirugía. De acuerdo al análisis bibliográfico y en relación a la opinión de los expertos se establece para el tratamiento de la reganancia los siguientes objetivos.

Objetivo general: la labor terapéutica del psicólogo bariátrico será reorientar y acompañar a las personas en el tratamiento para lograr una mayor adherencia al mismo.

Objetivos específicos se centraran en determinar y analizar las posibles causas psicológicas de reganancia de peso; identificar factores socio ambientales y familiares que pueden influenciar como predictores de la recuperación de peso; incorporar dispositivos individuales y grupales que favorezcan el descenso de peso y su mantenimiento a través de generar cambios de hábitos entre otros.

El psicólogo bariátrico deberá:

1. Realizar seguimiento de las personas con tratamiento quirúrgicos de la obesidad a fin detectar posible reganancia de peso.
2. Promover y derivar a control clínico - quirúrgico para descartar causas clínicas o relacionadas a complicaciones quirúrgicas
3. Evaluar la adherencia de los pacientes y modificaciones del estilo de vida. Es importante analizar si está realizando los controles con el equipo interdisciplinario, cada cuánto tiempo, si ha realizado cambios en la implementación de nuevos hábitos como los relacionados con la alimentación y la actividad física.
4. Determinar posibles causas de reganancia. Es necesario revisar la valoración previa a cirugía,

detectar aspectos negativos no detectados anteriormente y otros que pudieran aparecer. O llevar a cabo una nueva revaloración psicológica.

5. Favorecer la comprensión de las causas que determinaron un aumento de peso. Es necesario que la persona pueda entender estas causas.

6. Evaluar complicaciones psicológicas. Se debe valorar posibles estados psicológicos que pueden estar influenciando el aumento de peso o manifestación patológica. La baja conciencia de enfermedad, trastornos de ansiedad mayor, estados de angustia, la baja tolerancia a la frustración, alteraciones en la imagen corporal pueden alterar la normal evolución post-quirúrgica

7. Analizar junto al profesional médico el uso de algunos medicamentos asociados al aumento de peso en especial si la persona ha iniciado tratamiento farmacológico psiquiátrico.

8. Involucrar a la familia o red de apoyo si es necesario

9. Hacer uso de las redes sociales o tecnología para estar en contacto con el paciente el mayor tiempo posible durante el postquirúrgico.

10. Es necesario brindar psico-educación, con respecto a los factores asociados al mantenimiento del peso, como son: mantener contacto con el equipo que realizó la cirugía, actividad física regular, conductas alimentarias saludables (desayunar, control de porciones, disminución en el consumo de grasa), control de las enfermedades emocionales, etc.

11. Las conductas que deben seguir con respecto al peso es: pesarse una vez a la semana (por la mañana, el mismo día, de manera indefinida). Establecer metas a corto plazo.

12. El abordaje de la alimentación incluye un automonitoreo de conductas, hábitos, etc. Favorecer la adherencia al plan alimentario para volver a perder peso, identificando las barreras y obstáculos que han encontrado a lo largo del proceso de reganancia de peso. Habrá que revisar si tendría beneficios la utilización de fármacos que disminuyan el hambre. Volver a incentivar al uso de estrategias conductuales (como el control de estímulos).

13. Desarrollar una imagen corporal positiva.

14. Reforzar la práctica de actividad física. Esta es una conducta indispensable para evitar la recuperación del peso perdido.

15. Analizar las expectativas de la persona operada en relación al peso

16. Crear un plan de prevención de recaídas. Que puede incluir: a) Mantener la calma (no dramatizar), b) Reconocer la vulnerabilidad: vacaciones, enfermedades, comer fuera de casa, ingesta emocional, c) Analizar la situación de recaída, d) Hacer un cambio inmediatamente, e) Organizar el plan, f) Revisar las razones para perder peso, g) Pedir ayuda (no perder el contacto con el equipo que lo operó).

Conclusión

La obesidad es una enfermedad crónica que requiere un control permanente de la patología. El tratamiento quirúrgico de la obesidad permitió a un gran porcentaje de pacientes con obesidad mórbida controlar su enfermedad y mejorar su calidad de vida. No obstante existe un porcentaje menor de personas con cirugía bariátrica que se alejan de los objetivos del tratamiento y es necesario brindar desde la psicología bariátrica un espacio de contención terapéutica que permita reorientar el tratamiento y acompañar a las personas a readaptarse nuevamente a un nuevo estilo de vida.

Conflictos de intereses

Los autores declaran no tener conflictos de interés, en relación a este artículo.

Bibliografía

1. Lauti M, Kularatna M, Hill AG, MacCormick AD. Weight Regain Following Sleeve Gastrectomy—a Systematic Review. *Obes Surg.* (2016) Jun; 26(6):1326-34. doi: 10.1007/s11695-016-2152-x.
2. Pataky, Z., Carrard, I., & Golay, A. (2011). Psychological factors and weight loss in bariatric surgery. *Current opinion in Gastroenterology*, 27(2), 167-173.
3. Odom, J., Zalesin, K. C., Washington, T. L., Miller, W. W., Hakmeh, B., Zaremba, D. L., ... & Chengelis, D. L. (2010). Behavioral predictors of weight regain after bariatric surgery. *Obesity surgery*, 20(3), 349-356
4. Rutledge, T., Groesz, L. M., & Savu, M. (2011). Psychiatric factors and weight loss patterns following

gastric bypass surgery in a veteran population. *Obesity surgery*, 21(1), 29-35.

5.Stoklossa CJ, Atwal S. Nutrition Care for Patients with Weight Regain after Bariatric Surgery. *Gastroenterology Research and Practice* 2013, 1-7. doi.org/10.1155/2013/256145.

6.Berti, L. V., Campos, J., Ramos, A., Rossi, M., Szego, T., & Cohen, R. (2015). Posição da SBCBM: nomenclatura e definições para os resultados em cirurgia bariátrica e metabólica. *ABCD Arquivos Brasileiros de Cirurgia Digestiva*,28(2).

7.Faria, S. L., de Oliveira Kelly, E., Faria, O. P., & Ito, M. K. (2009). Snack-eating patients experience lesser weight loss after Roux-en-Y gastric bypass surgery. *Obesity surgery*, 19(9), 1293-1296.

E. Coêlho BM, Santana GL, **Duarte-Guerra LS**, Viana MC, Lotufo-Neto, Andrade LH, Wang YP. The role of gender in the structure of networks of childhood adversity. *Psychiatry Research*. 2018. doi: <https://doi.org/10.1016/j.psychres.2018.09.059>.

Reprinted by permission by Psychiatry Research
from Elsevier and Copyright Clearance Center.
License Number: 4446100375749

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

The role of gender in the structure of networks of childhood adversity

Bruno Mendonça Coêlho^{a,b,*}, Geilson Lima Santana^a, Leorides Severo Duarte-Guerra^a, Maria Carmen Viana^c, Francisco Lotufo Neto^b, Laura Helena Andrade^a, Wang Yuan-Pang^a^a Núcleo de Epidemiologia Psiquiátrica (LIM-23), Instituto de Psiquiatria, Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil^b Departamento de Psiquiatria, Faculdade de Medicina (FMUSP), Universidade de São Paulo, São Paulo, SP, Brazil^c Department of Social Medicine Post-Graduate Program in Public Health, Health Sciences Center, Universidade Federal do Espírito Santo, Vitória, ES, Brazil

ARTICLE INFO

Keywords:

Network analysis
Childhood adversities
Gender difference
Risk factor
Mental disorders
Epidemiology

ABSTRACT

The objective of present study is to investigate the relationship between different childhood adversities. The potential impact of early adversity on prevention programs is discussed. Data on twelve childhood adversities was collected from a representative sample of 5037 members of the general population living in a large metropolitan area. Data were analyzed through network analysis, to estimate and compare network connectivity and centrality measures by gender. Over half the respondents had been exposed to at least one adversity during their earlier developmental stage. Among adversity-exposed persons, 48.4% presented simultaneous adversities, most of which were related to 'family dysfunction' and 'maltreatment' (mean = 2.9 adversities). Women reported more adversities than men (59.0% vs. 47.6%). Although the 'global' network connectivity across adversities was similar in both genders, 'regional' distinctions in the network structure were found. While 'neglect' and 'parental death' were more important for women than men, 'parental mental disorders' was more important for men. Gender-related childhood adversities were clustered experiences. Adversities related to 'early family dysfunction' and 'maltreatment' were prominent features in the networks of both boys and girls. Differential preventive and intervention programs should take into account gender-related patterns of exposure and reporting patterns of early adversity.

1. Introduction

There are several stressors linking kinds of trauma *a priori*, e.g., natural, human, fateful stressors, with human psychopathology (Dohrenwend, 2000; Levine et al., 2016; Weinstein et al., 2018). Among them, childhood adversities—or adverse childhood experiences—are unfavorable experiences that may occur to individuals early in life, being common risk factors in general population (Coêlho et al., 2016; Kessler et al., 2010). The literature has indicated that exposure to childhood adversities is associated with direct and indirect protracted aftermaths. Different childhood adversities has been implicated with outcomes such as enduring medical consequences (e.g. headache, respiratory or thyroid disease) (Lee et al., 2009; Sheikh, 2018a); psychopathology in adulthood—e.g. mood disorders, post-traumatic stress disorder (PTSD), and psychosis (Kessler et al., 2010; Morgan and Gayer-Anderson, 2016); suicidality (Bruffaerts et al., 2010; Coêlho et al., 2016), premature death (Brown et al., 2009), and even subjective experiences such as dissatisfaction with friendships in adulthood

(Sheikh, 2018b).

Previous studies suggested the effect of childhood adversities differ by gender (Almuneef et al., 2017; Gershon et al., 2008). Girls are more affected by 'negligence', 'emotional abuse', 'household dysfunction', 'sexual abuse' (Benjet, 2010; Benjet et al., 2009; Evans et al., 2017; Hua et al., 2014; Koenig and D'Souza, 1986) and more exposed and 'physical abuse' than boys (Sheikh et al., 2016b). Conversely, boys are more affected by 'parental mental disorders', 'parental divorce' (Amato, 2001; Amato and Keith, 1991; Tronick and Reck, 2009), and 'psychological abuse' (Sheikh et al., 2016b).

It is possible to distinguish a distinct difference in profile of exposure to adversity between boys and girls. Boys present a three-factor underlying structure, while girls present a two-factor structure (Coêlho et al., 2018). Therefore, it is judicious to suppose that such differences could be attributed to gender-related cognitive vulnerability, exposure liability and coping strategy in the face of stressful incidents, such as childhood adversities (Hankin and Abramson, 2001; Hyde et al., 2008; Nolen-Hoeksema and Girgus, 1994). Some plausible

* Corresponding author at: Núcleo de Epidemiologia Psiquiátrica (LIM-23), Instituto de Psiquiatria do Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo, Rua Dr. Ovídio Pires de Campos, 785, CEP 05403-010 São Paulo, SP, Brazil.

E-mail address: bmcuelho@usp.br (B.M. Coêlho).

<https://doi.org/10.1016/j.psychres.2018.09.059>

Received 5 April 2018; Received in revised form 16 August 2018; Accepted 25 September 2018

Available online 26 September 2018

0165-1781/ © 2018 Elsevier B.V. All rights reserved.

Table 1
Descriptive characteristics of the participants of São Paulo Megacity Mental Health Survey (*N* = 5037).

Variable	<i>n</i>	%
Gender		
Male	2187	43.42
Female	2850	56.58
Age, years		
18–29	1287	25.55
30–39	1193	23.68
40–49	1090	21.64
50 or more	1467	29.12
Education (years of schooling)		
Low (0–4)	1344	26.68
Low-average (5–8)	1262	25.05
High-average (9–11)	1690	33.55
High (≥ 12)	741	14.71
Family income		
Low	1200	23.82
Low-average	1367	27.14
High-average	1212	24.06
High	1258	24.98
Marital status		
Married/cohabiting	3250	64.52
Previous married	894	17.75
Never married	893	17.73
Employment status		
Employed	3030	60.15
Student	56	1.11
Homemaker	836	16.60
Retired	494	9.81
Unemployed	621	12.33

of the participants may be found in Table 1. Briefly, participants were predominantly women (56.5%), married (64.5%) and currently employed (60.2%), with balanced distribution across educational levels, socioeconomic strata, and age brackets.

2.2. Ethics procedures

The investigation was executed according to the latest version of the Declaration of Helsinki. Respondents were interviewed only after the researchers had obtained informed written consent in which the nature of the procedures had been explained and confidentiality was assured. The Ethical and Research Committee of University of São Paulo Medical School approved the procedures.

2.3. Assessment tools

The World Mental Health Survey version of the Composite International Diagnostic Interview (WMH-CIDI) was used, generating diagnoses by DSM-IV criteria. This is a fully structured interview, applied face-to-face by trained lay interviewers (Viana et al., 2004). The WMH-CIDI has two parts: the first, administered to all subjects, embraces core diagnostic sections (e.g.: major depression, panic disorders, suicidal behavior), demographic information, daily functioning, and physical morbidity.

Part 2 contains questions about risk factors, consequences, and other correlates, assessing additional disorders, and was administered to all respondents with lifetime criteria for any Part 1 disorder, plus a probability subsample of other subjects in order to reduce the burden for respondents and control study costs ($n = 2.942$). The instrument allows for 20 possible diagnoses: major depression, bipolar I and II disorders, dysthymia, panic disorder, agoraphobia, social phobia, specific phobia, childhood and adult separation anxiety disorders, generalized anxiety disorder, PTSD, alcohol and drug abuse and dependence, intermittent explosive disorder, oppositional-defiant disorder, conduct disorder and attention-deficit/hyperactivity disorder. It also assesses the age-of-onset of these disorders through questions designed

to improve the accuracy of retrospective reports and avoid implausible response patterns (Simon and VonKorff, 1995).

The WMH-CIDI assessed socio-demographic correlates and childhood adversities, which encompass 12 dichotomous (yes/no) variables that respondents may have experienced before the age of 18 (Green et al., 2010). Further details on World Mental Health Survey coding and data collection have been described elsewhere (Green et al., 2010; Kessler et al., 2010; Lee et al., 2011).

Childhood adversities were divided into four groups according with experience type, as suggested by previous studies: (a) parental maladjustment (parental mental illness, parental substance misuse, parental criminality, and family violence); (b) maltreatment or abuse/neglect (physical abuse, sexual abuse, neglect); (c) biological and non-biological parental loss (parental death, parental divorce, and other parental loss), and (d) other childhood adversities (life-threatening physical illness and economic adversity) (Kessler et al., 2010).

The WMH-CIDI section on childhood adversities includes several instruments that were used in this study: (1) The Family History Research Diagnostic Criteria Interview: assessed parental mental illness and parental substance misuse (Endicott et al., 1978); (2) measures created for the National Comorbidity Survey (NCS) and used in similar surveys (Benjet et al., 2010; Kessler et al., 2010): assessed parental criminality (Kessler et al., 1997); (3) the Conflict Tactics Scale modified version (Straus, 1979): assessed physical abuse and family violence—experiences including beating, slapping, hitting, pushing, grabbing/shoving/throwing something at the child—committed by father, mother (biological, step- or adoptive parents), and/or by those who nurtured the minor; (4) questions commonly used in child welfare studies: assessed parental neglect (frequency of having inadequate supervision, performs age-inappropriate tasks, jobs or chores, or having inadequate food, clothing or medical care); (5) questions about repeated fondling, attempted rape or rape (including complete intercourse, penetration by finger or object, sexual assault or molestation): assessed sexual abuse (Molnar et al., 2001); (6) measures created for the NCS and used in similar surveys (Benjet et al., 2010; Kessler et al., 2010): assessed parental loss, including parental death, divorce/separation, and other losses (Kessler et al., 1997). ‘Other parental losses’: assessed parental absence for six months or more for reasons other than separation/divorce (e.g. due to overseas service, imprisonment, hospitalization, etc.); (7) a standard chronic conditions checklist assessed: life-threatening physical illness; and (8) measures created for the NCS assessed: economic adversity through questions on family ability to pay for basic necessities of life or on family receipt of government assistance during childhood (Kessler et al., 1997).

2.4. Statistical analysis

First the prevalence and distribution of childhood adversities was estimated. The Taylor series linearization method [SUDAAN software (RTI, 2002)] was used to generate results from this complex sample and to weight and estimate standard errors for proportions of participants who had experienced childhood adversities.

Network analyses were used to estimate the relationship between childhood adversities for both genders. This method was designed to evaluate the relationship between dichotomic variables. The networks were generated by the enhanced Least Absolute Shrinkage and Selection Operator (eLASSO) (van Borkulo et al., 2014). Association between pairs of variables were calculated by combining the extended Bayesian Information Criterion (EBIC) (Foygel and Drton, 2010, 2015) and L1-regularized logistic regression analysis shrinking irrelevant estimates to zero to obtain an ideal trade-off between model goodness-of-fit and sparsity (Tibshirani, 1996). For interpretation, if tuning parameter λ (λ) of LASSO is high, many edges are removed minimizing spurious connections (Foygel and Drton, 2010, 2015). These procedures are implemented in the R package “IsingFit”.

To adjust for sampling weights, the parameter “weight” (sampling

weights vector) was introduced in the *glmnet* function used by the *IsingFit* function and this altered *IsingFit* function is known as “*IsingFit_weights*”. The EBIC hyperparameter γ (*gamma*) was adjusted to 0.25 generating a less spuriously connected model and maintaining such real connections as existed (Foygel and Drton, 2010; van Borkulo et al., 2014). The R package *qgraph* generated the network visualization. All step-by-step R commands are described at <http://sachaepskamp.com/files/Cookbook.html>.

Low occurrence of some adversities occurred in the men's subgroup. All analyses were performed after the exclusion of ‘sexual abuse’, ‘economic adversity’, and ‘physical illness’. Similar exclusions were implemented in the women's networks allowing between-gender comparability.

Centrality measures were obtained to quantify the degree of connectivity among nodes: (a) *node strength*, reflects the degree to which a certain node is involved in the network by measuring its weighted number of connections (Barrat et al., 2004), (b) *betweenness*, assesses the degree to which a node lies on the shortest path between two other nodes (Opsahl et al., 2010), and (c) *closeness*, defined as the inverse sum of shortest distances to all other nodes from a focal node (Opsahl et al., 2010). In summary, these measures indicate how connected the childhood adversities (nodes) are: high values for all three indicate that a particular node (childhood adversity) plays a central role in the network, is very connected with others childhood adversities, acts like a ‘bridge’ between childhood adversities and is well placed to influence the entire network.

The network comparison test (NCT), a permutation test for between-network differences, compared the structure and global level (or strength) of connections between the networks of each gender (Van Borkulo, 2015), and is implemented in the R package NCT. To adjust for sampling weights, the NCT function was also changed: the “*IsingFit_weights*” function surrogated the original *IsingFit* function. The gender-specific values for each edge were computed two-by-two through NCT by means of 36 multiple comparisons to assess significant differences. The value of each edge, for example, between ‘physical abuse’ and ‘neglect’ or ‘physical abuse’ and ‘parental death’, was calculated in each one of the networks that were randomly simulated, and compared between genders, also allowing generation of a probability distribution.

The bootstrap method, with 1000 resamplings for each gender, ascertained which variables were most distinguished among the networks. Differences of three between-gender centrality measures and Cohen's effect sizes (ES) were calculated. For interpretation, ES greater than 0.5 were considered medium, while those greater than 0.8, were considered large (Coe, 2002). Positive values indicated values greater for women's network than for men's network, and negative values indicated that the values were greater for the men's network than for women's network.

Data weighting procedures for variance estimation with complex sample survey data took account of the stratified multi-stage sample design used. A post-stratification weight was used to achieve a sample distribution, on a cross-classification of socio-demographic variables for the population distribution in the 2000 Census. Additional weight adjusted for different within-household probability of selection and non-response. Further details of the weighting procedures can be found elsewhere (Viana et al., 2009). Two-tailed 0.05-level test evaluated statistical significance.

3. Results

3.1. Distribution of childhood adversities

The lifetime prevalence of childhood adversities was 53.6% (Table 2). Almost half of the sample (48.4%) presented two or more adversities, with ‘sexual abuse’, and ‘economic adversity’ the most frequently co-occurring. Mean number of adversities of those with

multiple childhood adversities was 2.9 (range: 2.9–3.6), favoring the modeling of these early-life phenomena into meaningful clustering patterns.

Regarding differential exposures to adversities by gender, women experienced more childhood adversities than men (59.0% vs. 47.66%, $p < 0.0001$). The following specific adversities were more prevalent ($p < 0.0001$) among women than men: ‘sexual abuse’ (1.2 vs. 0.1%), ‘neglect’ (14.1 vs. 8.1%), ‘other parental loss’ (11.0 vs. 5.5%), ‘family violence’ (15.5 vs. 8.4%), and ‘parental mental disorders’ (14.4 vs. 9.0%). This psychopathological consistency favored investigation of adversities by gender.

3.2. Network structure

The network structure for both genders is shown in Fig. 1. Adversities of the same group were placed sequentially for inspection (network ‘circle’ visualization). Three groups of childhood adversities proposed by previous studies—interpersonal loss, parental maladjustment and maltreatment—were consecutively shown in nodes of the same color. Such visualization allows a better appraisal of the connection strength between the variables, although it does not take into account the centrality of the nodes or the distance between them.

As expected, dysfunctional family structure signified the likelihood of early exposure to adversities for both genders. However, the strongest between-variable edges shown for women were ‘family violence’ and ‘parental substance use’ (edge value [EV] = 1.60), and between ‘physical abuse’ and ‘neglect’ (EV = 1.40). Conversely, the strongest between-variable edges shown for men were between ‘family violence’ and ‘physical abuse’ (EV = 1.73), and between ‘parental substance use’ and ‘parental criminality’ (EV = 1.45). For both genders, the inverse connection between ‘parental death’ and ‘parental divorce’ was the only negative association (red edge).

Comparing women and men's network strength, both presented similar connectivity ($p = 0.46$; global strength indicator of 15.44 vs. 13.58, respectively). Likewise, in two-by-two comparisons of adversities by gender, no significant differences emerged for analogous connections.

Fig. 2 shows the network ‘spring’ visualization, providing an alternative appraisal of the relationships between variables, since it takes into account the centrality and the distance between the nodes. Accordingly, adversities with higher *strength*, *betweenness* and *closeness* values or more relevance to the network—such as ‘family violence’ and ‘parental substance use’—were placed more centrally.

3.3. Centrality indexes

Regarding centrality indexes, ‘family violence’ and ‘physical abuse’ presented the highest values for *betweenness*, *closeness* and *node strength* indexes in both genders (Fig. 3). ‘Parental substance use’ presented the highest values for *closeness*, and *node strength* in both genders.

Table 3 shows the average difference between women and men's centrality indicators, as well as the effect size. Concerning gender differences, women presented significantly higher values than men for ‘neglect’ in *strength* and *betweenness* indexes (effect sizes [ES] = 1.5583, and 1.4594, respectively). Additionally, ‘parental death’ presented higher values in *strength* (ES = 0.8115).

Conversely, men had higher *betweenness* and *strength* than women for ‘parental mental disorders’ (ES = −0.8045, and −1.1010, respectively), and *betweenness* for ‘parental divorce’ (ES = −0.9004). The *strength* of ‘parental divorce’ had moderate ES (−0.7525) (Table 3). The overall structure indicated that ‘family violence’ and ‘neglect’ were the most important variables for the network, and the most prominent variables presenting gender difference.

Table 2Weighted prevalence and distribution of childhood adversities (CA) in the total sample, in the sample with any adversities and by gender ($N = 5037$).

	Prevalence of adversity			<i>p</i>	Among those with any CA: % with 2+ adversities	Mean number of CA among those with 2+ adversities
	Total	Women	Men			
Childhood adversities	% (SE)	% (SE)	% (SE)		% (SE)	% (SE)
<i>I. Abuse/neglect</i>						
Physical abuse	16.0 (1.1)	17.4 (1.5)	14.4 (1.6)	0.327	73.7 (3.3)	3.0 (0.1)
Neglect	11.3 (0.9)	14.1 (1.3)	8.1 (1.1)	<0.0001	85.8 (2.2)	3.2 (0.1)
Sexual abuse	0.7 (0.2)	1.2 (0.3)	0.1 (0.1)	<0.0001	95.2 (2.7)	3.0 (0.2)
<i>II. Interpersonal loss</i>						
Parental death	16.1 (1.0)	16.8 (1.1)	15.3 (1.7)	0.102	47.1 (4.2)	3.2 (0.1)
Parental divorce	9.5 (0.7)	10.8 (0.9)	8.0 (1.2)	0.444	60.7 (4.3)	3.4 (0.1)
Other parent loss	8.4 (0.9)	11.0 (1.3)	5.5 (0.6)	<0.0001	73.8 (3.0)	3.6 (0.1)
<i>III. Family psychopathology</i>						
Family violence	12.1 (0.8)	15.5 (1.3)	8.4 (1.0)	<0.0001	87.5 (2.3)	3.4 (0.1)
Parental mental disorders	11.8 (0.9)	14.4 (1.3)	9.0 (1.0)	<0.0001	76.9 (2.5)	3.2 (0.1)
Parental substance use	9.7 (0.9)	11.6 (1.3)	7.7 (1.3)	0.090	78.3 (3.5)	3.6 (0.1)
Parental criminal behavior	3.6 (0.4)	4.3 (0.6)	2.7 (0.7)	0.831	89.1 (4.1)	3.4 (0.2)
<i>IV. Other adversities</i>						
Physical illness	1.4 (0.4)	0.8 (0.2)	2.1 (0.6)	0.267	62.2 (13.1)	3.0 (0.2)
Economic adversity	1.0 (0.2)	0.9 (0.2)	1.0 (0.3)	0.467	94.4 (2.9)	2.9 (0.2)
Any adversity	53.6 (1.8)	59.0 (1.7)	47.6 (3.2)	<0.0001	48.4 (1.5)	2.9 (0.1)

Fig. 1. “Circle” visualization of network structure of females (left panel; $n = 2850$) and males (right panel; $n = 2187$). Note: Green connections represent positive association, whereas red connections represent negative association between the adversities. The thicker the line (edge), the stronger is the association (positive or negative) between the variables (nodes). *phy* indicates physical abuse; *ngl*, neglect; *prd*, parental death; *pdv*, parental divorce; *opr*, other parent loss; *fmv*, family violence; *pmn*, parental mental disorders; *prs*, parental substance use; *prc*, parental criminal behavior. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

4. Discussion

In the last three decades, childhood adversity has become an important topic in psychiatric research, shifting the paradigm of the

medical community approach to understand diseases. Childhood adversities are a cluster of consistently highly interconnected experiences and ‘family violence’, ‘neglect’, ‘parental substance use’ and ‘physical abuse’ were the most central adversities in the networks for both

Fig. 2. “Spring” visualization of network structure of females (left panel; $n = 2850$) and males (right panel; $n = 2187$). Note: Green connections represent positive association, whereas red connections represent negative association between the adversities. The thicker the line (edge), the stronger is the association (positive or negative) between the variables (nodes). The closer the distance between two variables (nodes), the more likely associated are the variables. *phy* indicates physical abuse; *ngl*, neglect; *prd*, parental death; *pdv*, parental divorce; *opr*, other parent loss; *fmv*, family violence; *pmn*, parental mental disorders; *prs*, parental substance use; *prc*, parental criminal behavior. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

legend, the reader is referred to the web version of this article.)

Fig. 3. Comparison of centrality indices of network analysis by gender. Note: *Betweenness*, assesses the degree to which a node lies on the shortest path between two other nodes (Opsahl et al., 2010); *Closeness*, is defined as the inverse sum of shortest distances to all other nodes from a focal node (Opsahl et al., 2010); *Strength*, reflects the degree to which a certain node is intricate in the network by measuring its weighted number of connections (Barrat et al., 2004). * represent a between-gender large effect size (>0.8), and † represent a between-gender medium effect size (>0.5 and ≤ 0.8). *phy* indicates physical abuse; *ngl*, neglect; *prd*, parental death; *pdv*, parental divorce; *opr*, other parent loss; *fmv*, family violence; *pmn*, parental mental disorders; *prs*, parental substance use; *prc*, parental criminal behavior.

distance use; *prc*, parental criminal behavior.

genders, indicating that they are the most important variables in the whole network. Although both genders presented similarly connected networks regarding global strength, there were some dissimilarities in individual adversities that emerged concerning their network arrangement and role. Notably, 'neglect' and 'unreliable parenting' presented differences between genders. To our knowledge, this is the first time network analysis has been applied to investigate childhood adversities in a large household sample. This investigation has provided a comprehensive demonstration of interrelationships between negative experiences individuals may undergo early in life and may contribute to tailoring preventive strategies for dysfunctional families. Intervention programs to improve family cohesion and parental coping skills may impact modifiable experiences, mitigating long-lasting risky environments, and promoting healthy development. The applicability of these findings remains to be investigated in future studies.

Previous investigations on three core clusters of childhood adversities—interpersonal loss, parental maladjustment and parental maltreatment—have made clinical inferences based merely on psychopathological observations (Kessler et al., 2010), without determining the whole complexity of interdependent adversities. In the present analysis, the results have shown how adversities are organized in comprehensive networks and the extent to which some central experiences may influence subordinate ones, e.g. while parental maladjustment and maltreatment were closely related, parental loss was more segregated. Possibly, this configuration can reflect shared cultural environments for distinct childhood adversities (Chang et al., 2013).

Previous research has demonstrated that having a dysfunctional or violent family is the most distressing feature in daily life during childhood (Green et al., 2010; McLaughlin et al., 2010). Since childhood adversities tend to co-occur, a single adversity may initiate a perpetuating cycle of worsening liability and hardships in early life (Dong et al., 2004; Kessler et al., 2010; Morgan and Gayer-Anderson, 2016). 'Family violence', for example, has been described as a robust predictor of exposure to numerous hazardous experiences (McGavock and Spratt, 2017). This cascade may generate additional exposures to other stressful events before adulthood, such as 'parental criminality', 'neglect', and 'parental divorce', as we showed in both networks. So, proper identification and timely intervention of gender-specific 'central' adversities can halt the cascade of unfavorable events in at-risk individuals.

'Neglect' was significantly 'central' to the whole relationships network. It was also the most 'in-between' path to other adversities among women, which shows that 'neglect' was the main bridge between two other adversities. Among men, 'parental mental disorder' was the most 'central' adversity. In terms of *betweenness*, or the role as a link between two other adversities, 'parental divorce' and 'parental mental disorders' were more relevant for men than women. The effect size of these differences supports the disparity between gender measures. Conclusive affirmation of these differences is challenging (Kraemer, 2000). The results could reflect cultural influences, behavioral characteristics, or a gene-environmental interaction. Girls tend to be more affected by negligence than boys in social circumstances where boys are highly

Table 3

Average difference and effect sizes distinctions for mean centrality indexes between women and men.

Node	Average Difference			Effect Size		
	Betweenness	Closeness	Strength	Betweenness	Closeness	Strength
Physical Abuse	-1.1440	0.0086	-0.0719	-0.1671	0.3117	-0.1134
Neglect	9.9260	0.0132	0.9326	1.4594*	0.4886	1.5583*
Parental Death	-0.2900	0.0062	0.5204	-0.0891	0.3392	0.8115*
Parental Divorce	-4.9700	-0.0014	-0.7425	-0.9004*	-0.0597	-0.7525†
Other Parent Loss	-1.6840	0.0063	0.2515	-0.3483	0.3205	0.3816
Family Violence	-1.8440	0.0059	0.0729	-0.2443	0.2010	0.0990
Parental Mental Disorders	-2.2540	-0.0003	-0.5943	-0.8045*	-0.0129	-1.1010*
Parental Substance Use	-0.3920	0.0087	0.0775	-0.0691	0.3310	0.1241
Parental Criminal Behavior	-0.1820	0.0051	0.2129	-0.1004	0.2359	0.3154

Note: * represent a between-gender large effect size (>0.8), and † represent a between-gender medium effect size (>0.5 and ≤ 0.8) (Coe, 2002). The red color values indicate that the effect size favors women; and the blue color values favors men.

Betweenness, assesses the degree to which a node lies on the shortest path between two other nodes (Opsahl et al., 2010); *Closeness*, is defined as the inverse sum of shortest distances to all other nodes from a focal node (Opsahl et al., 2010); *Strength*, reflects the degree to which a certain node is intricate in the network by measuring its weighted number of connections (Barrat et al., 2004).

valued, e.g. in Asian cultures (Hua et al., 2014; Koenig and D'Souza, 1986). This also seems to apply in Latin cultures such as Brazil, where male sexism still prevails (Zanatta et al., 2016). Likewise, boys are more affected than girls by 'parental divorce' (Amato, 2001; Amato and Keith, 1991) and by 'parental mental disorders' (Tronick and Reck, 2009) in patriarchal societies, where there are more demands for men to be tough and act as the family provider (Kraemer, 2000).

The main clinical significance of this study is the necessity of developing multidimensional comprehensive strategies—using joint teams involving social workers, psychologists, law counselors, nurses, and psychiatrists—to prevent and ameliorate childhood adversities. Recently, the concept of syndemicity (Singer, 2000) was highlighted in public health literature (Mendenhall, 2017; Singer et al., 2017) to understand the circumstances in which multiple diseases occur. This theoretical approach underlines the context in which individuals live in low-income and middle-income country settings (Mendenhall et al., 2017), alongside the relationship between comorbidities. Evidence-based preventive programs on child abuse and neglect, such as the U.S. Preventive Services Task Force recommendation statement and the WHO guideline to prevent child maltreatment, are scarce (Butchart et al., 2006; Moyer and United States Preventive Services Task Force, 2013). Generally, prevention comprises early identification and intervention to protect the victims. Nevertheless, they have shown little impact on large-scale reduction of childhood adversities incidence (Butchart et al., 2006), since they are typically focused on only a group of adversities. Programs aiming to improve the care of children can change the way parents accomplish that, although their efficiency differs by program and model of intervention (Fortson et al., 2016; Portwood et al., 2011). However, they cannot change unexpected childhood adversities such as 'parental mental disorder' or 'parental death'.

Appropriate interventions should focus on the central childhood adversities, but also act on other adversities in the network. Furthermore, the existing programs on childhood adversities, and medical and public health research are generally not gender driven (Fortson et al., 2016), despite the evidence suggesting gender-specific characteristics of disease organization (Chmiel et al., 2014; Kalgotra et al., 2017). Nevertheless, our findings reinforce the indication that gender should be considered in the elaboration of such programs. The use of comprehensive novel methodologies to study childhood adversities is an utmost necessity to grasp the intricacy of these risk factors. For example, 'neglect', represents an important pathway between other adversities, having a differential role by gender as an in-between path to other childhood adversities associated with later outcomes. So, gender-specific adjustments are mandatory to create gender-focused programs.

Ideally, the impact of the network approach would be strengthened if later adult psychopathology could be associated with centrality indicators. However, network indicators were calculated observing the whole network, rather than person-based ones. So, this promising configuration of childhood adversities should be replicated with a prospective design.

There were some limitations to our findings. First, it is not possible to infer causal direction of pathways with cross-sectional data. However, it was possible to study the comorbidity pattern of childhood adversities allowing a better understanding of their interaction than achieved with previous methods, suggesting directions for intervention, and future intervention research. Second, individuals tend to under-report painful or shameful experiences (Hardt and Rutter, 2004), and the style of the assessment questions ("yes/no") could enable respondents to overlook or emphasize some life events. Third, recall bias might have occurred due to the time elapsed between exposure to childhood adversities and their assessment. Furthermore, men and women report life events differently, possibly affecting the prevalence of adversities by gender (Coêlho et al., 2018; Sheikh et al., 2016b). Future approaches for examining this response pattern might be refined

through a two-parameter logistic (2-PL) item response theory model, to account for the discrimination estimate of each included childhood adversity (Baker, 1985; Rasch, 1980). Since under-reporting may have occurred for some adversities, specific associative relationships can be weaker. Therefore, for those low prevalence and non-disclosed adversities, the precision of association will be jeopardized. Acknowledging these biases, the estimated prevalence of under-reported childhood adversities should be considered conservative, generating networks with fewer connections. On the other hand, some enduring emotions may counterbalance the recall bias, persisting for decades after exposure to the adversity. Fourth, although only 12 adversities were assessed, other events may have occurred earlier (Kessler et al., 1997) jeopardizing further meaningful analysis. Finally, no longitudinal prediction was tested in the resulting models, being the focus of a forthcoming investigation.

Network analysis has disentangled the multifaceted interplay between early-life adversities. Childhood adversities are an important group of interconnected experiences associated with lifetime psychopathology. Adversities related to early family dysfunction and maltreatment were the prominent features in the adversities network, potentially influencing the development of other adversities. Beyond looking at specific adversities, e.g., physical abuse, attentive educators and policy makers should contemplate the whole environment where these experiences have occurred. Furthermore, these results reinforced the need for a revised list of adversities addressed in the literature.

Boys and girls presented similar global connectivity patterns, whereas regional dissimilarities were observed in the structure of the networks. Consequently, gender-centered interventional public health programs must consider the interconnected structure. Notably, 'neglect' and adversities related to unreliable parenting might impede an individual's development. These findings take into account the gender-differences that occur in the reporting of childhood experience. Longitudinal investigations of the trajectory of people who experienced childhood adversities are necessary to demonstrate long-term effects in the development of other adversities and health outcomes.

Conflict of interest statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Acknowledgments and funding

The São Paulo Megacity Mental Health Survey was funded by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, São Paulo Research Foundation; Grant nos. 2003/00204-3, and 2011/50517-4; <http://www.fapesp.br/materia/176/projeto-tematico/projeto-tematico.htm>). Instrument development was supported by Fundo de Apoio à Ciência e Tecnologia do Município de Vitória (FACITEC, Vitória Municipal Science and Technology Fund; Grant no. 002/2003) in the state of Espírito Santo, Brazil. Dr. Laura H. Andrade is supported by a grant from the Brazilian Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, National Council for Scientific and Technological Development; Grant no. 307623/2013-0). The São Paulo State Department of Public Safety supported the sub-project on violence and trauma. The São Paulo Megacity Mental Health Survey was carried out in conjunction with the World Health Organization World Mental Health (WMH) Survey Initiative. The authors thank the WMH staff for assistance with instrumentation, fieldwork, and data analysis. The authors declare that the funders of the São Paulo Megacity Mental Health Survey had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. We also thank Miss. Aline Damascena, B.A., M.Sc. for statistical advices.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2018.09.059.

References

- Almuneef, M., ElChoueiry, N., Saleheen, H.N., Al-Eissa, M., 2017. Gender-based disparities in the impact of adverse childhood experiences on adult health: findings from a national study in the Kingdom of Saudi Arabia. *Int. J. Equity Health* 16 (1), 90.
- Amato, P.R., 2001. Children of divorce in the 1990s: an update of the Amato and Keith (1991) meta-analysis. *J. Fam. Psychol.* 15 (3), 355–370.
- Amato, P.R., Keith, B., 1991. Parental divorce and the well-being of children: a meta-analysis. *Psychol. Bull.* 110 (1), 26–46.
- Baker, F.B., 1985. The Basics of Item Response Theory. Heinemann, Portsmouth, NH.
- Barrat, A., Barthélemy, M., Vespignani, A., 2012. Dynamical Processes on Complex Networks, reprint ed. Cambridge University Press, Cambridge.
- Barrat, A., Barthélemy, M., Pastor-Satorras, R., Vespignani, A., 2004. The architecture of complex weighted networks. *Proc. Natl. Acad. Sci. USA* 101 (11), 3747–3752.
- Barrett, P.T., Kline, P., 1981. The observation to variable ratio in factor analysis. *Pers. Study Group Behav.* 1, 23–33.
- Beard, C., Millner, A.J., Forgeard, M.J., Fried, E.I., Hsu, K.J., Treadway, M.T., Leonard, C.V., Kertz, S.J., Bjorgvinsson, T., 2016. Network analysis of depression and anxiety symptom relationships in a psychiatric sample. *Psychol. Med.* 46 (16), 3359–3369.
- Benjet, C., 2010. Childhood adversities of populations living in low-income countries: prevalence, characteristics, and mental health consequences. *Curr. Opin. Psychiatry* 23 (4), 356–362.
- Benjet, C., Borges, G., Medina-Mora, M.E., 2010. Chronic childhood adversity and onset of psychopathology during three life stages: childhood, adolescence and adulthood. *J. Psychiatr. Res.* 44 (11), 732–740.
- Benjet, C., Borges, G., Medina-Mora, M.E., Zambrano, J., Cruz, C., Mendez, E., 2009. Descriptive epidemiology of chronic childhood adversity in Mexican adolescents. *J. Adolesc. Health* 45 (5), 483–489.
- Brown, D.W., Anda, R.F., Tiemeier, H., Felitti, V.J., Edwards, V.J., Croft, J.B., Giles, W.H., 2009. Adverse childhood experiences and the risk of premature mortality. *Am. J. Prev. Med.* 37 (5), 389–396.
- Bruffaerts, R., Demyttenaere, K., Borges, G., Haro, J.M., Chiu, W.T., Hwang, I., Karam, E.G., Kessler, R.C., Sampson, N., Alonso, J., Andrade, L.H., Angermeyer, M., Benjet, C., Bromet, E., de Girolamo, G., de Graaf, R., Florescu, S., Gureje, O., Horiguchi, I., Hu, C.Y., Kovess, V., Levinson, D., Posada-Villa, J., Sagar, R., Scott, K., Tsang, A., Vassilev, S.M., Williams, D.R., Nock, M.K., 2010. Childhood adversities as risk factors for onset and persistence of suicidal behaviour. *Br. J. Psychiatry* 197 (1), 20–27.
- Butchart, A., Kahane, T., Harvey, A.P., Mian, M., Furniss, T., 2006. Preventing Child maltreatment: A Guide to Taking Action and Generating Evidence. WHO and International Society for the Prevention of Child Abuse and Neglect, Geneva.
- Chang, J., Natsuaki, M.N., Chen, C.N., 2013. The importance of family factors and generation status: mental health service use among Latino and Asian Americans. *Cultur. Divers. Ethnic Minor. Psychol.* 19 (3), 236–247.
- Chmielek, A., Klimek, P., Thurner, S., 2014. Spreading of diseases through comorbidity networks across life and gender. *New J. Phys.* 16 (11), 115013.
- Coe, R., 2002. It's the effect size, stupid: what "effect size" is and why it is important. In: 2002 Annual Conference of the British Educational Research Association. University of Exeter, Exeter, Devon, England.
- Côelho, B.M., Andrade, L.H., Borges, G., Santana, G.L., Viana, M.C., Wang, Y.P., 2016. Do childhood adversities predict suicidality? findings from the general population of the metropolitan area of Sao Paulo, Brazil. *PLoS One* 11 (5), e0155639.
- Côelho, B.M., Santana, G.L., Viana, M.C., Andrade, L.H., Wang, Y.P., 2018. Gender-related dimensions of childhood adversities in the general population. *Rev. Bras. Psiquiatr.* 40 (4), 394–402.
- Dohrenwend, B.P., 2000. The role of adversity and stress in psychopathology: some evidence and its implications for theory and research. *J. Health Soc. Behav.* 41 (1), 1–19.
- Dong, M., Anda, R.F., Felitti, V.J., Dube, S.R., Williamson, D.F., Thompson, T.J., Loo, C.M., Giles, W.H., 2004. The interrelatedness of multiple forms of childhood abuse, neglect, and household dysfunction. *Child Abuse Negl.* 28 (7), 771–784.
- Endicott, J., Andreasen, N., Spitzer, R.L., 1978. Family History Research Diagnostic Criteria. New York State Psychiatric Institute, New York, NY.
- Epskamp, S., Cramer, A., Waldorp, L., Schmittmann, V.D., Borsboom, D., 2012. qgraph: network visualizations of relationships in psychometric data. *J. Stat. Softw.* 48 (1), 1–18.
- Evans, E., Upchurch, D., Grella, C.E., 2017. Gender differences in the effect of childhood adversity on alcohol, drug, and poly-substance use disorders. *Drug Alcohol Depend.* 171, e60.
- Fortson, B.L., Kleven, J., Merrick, M.T., Gilbert, L.K., Alexander, S.P., 2016. Preventing Child Abuse and Neglect: A Technical Package for Policy, Norm, and Programmatic Activities. National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA.
- Foygel, R., Drton, M., 2010. Extended Bayesian information criteria for Gaussian graphical models. *Adv. Neural Inf. Process. Syst.* 23, 2020–2028.
- Foygel, R., Drton, M., 2015. High-dimensional Ising model selection with Bayesian information criteria. *Electron. J. Stat.* 9 (1), 567–607.
- Frewen, P.A., Schmittmann, V.D., Bringmann, L.F., Borsboom, D., 2013. Perceived causal relations between anxiety, posttraumatic stress and depression: extension to moderation, mediation, and network analysis. *Eur. J. Psychotraumatol.* 4 (1), 20656. <https://doi.org/10.3402/ejpt.v4i0.20656>.
- Gershon, A., Minor, K., Hayward, C., 2008. Gender, victimization, and psychiatric outcomes. *Psychol. Med.* 38 (10), 1377–1391.
- Goekoop, R., Goekoop, J.G., Scholte, H.S., 2012. The network structure of human personality according to the NEO-PI-R: matching network community structure to factor structure. *PLoS One* 7 (12), e51558.
- Green, J.G., McLaughlin, K.A., Berglund, P.A., Gruber, M.J., Sampson, N.A., Zaslavsky, A.M., Kessler, R.C., 2010. Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: associations with first onset of DSM-IV disorders. *Arch. Gen. Psychiatry* 67 (2), 113–123.
- Hankin, B.L., Abramson, L.Y., 2001. Development of gender differences in depression: an elaborated cognitive vulnerability-transactional stress theory. *Psychol. Bull.* 127, 773–796.
- Hardt, J., Rutter, M., 2004. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *J. Child Psychol. Psychiatry, Allied Discip.* 45 (2), 260–273.
- Hua, J., Mu, Z., Nwaru, B.I., Gu, G., Meng, W., Wu, Z., 2014. Child neglect in one-child families from Suzhou City of mainland China. *BMC Int. Health Hum. Rights* 14, 8.
- Hyde, J.S., Mezulis, A.H., Abramson, L.Y., 2008. The ABCs of depression: integrating affective, biological, and cognitive models to explain the emergence of the gender difference in depression. *Psychol. Rev.* 115 (2), 291–313.
- IBGE, 2001. Censo demográfico populacional do ano 2000. Instituto Brasileiro de Geografia e Estatística.
- Jenness, J.L., McLaughlin, K.A., 2015. Towards a person-centered approach to the developmental psychopathology of trauma. *Soc. Psychiatry Psychiatr. Epidemiol.* 50 (8), 1219–1221.
- Kalgotra, P., Sharda, R., Croff, J.M., 2017. Examining health disparities by gender: a multimorbidity network analysis of electronic medical record. *Int. J. Med. Inform.* 108, 22–28.
- Kelly, C.A., Soler-Hampejsek, E., Mensch, B.S., Hewett, P.C., 2013. Social desirability bias in sexual behavior reporting: evidence from an interview mode experiment in rural Malawi. *Int. Perspect. Sex Reprod. Health* 39 (1), 14–21.
- Kessler, R.C., Davis, C.G., Kendler, K.S., 1997. Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. *Psychol. Med.* 27 (5), 1101–1119.
- Kessler, R.C., McLaughlin, K.A., Green, J.G., Gruber, M.J., Sampson, N.A., Zaslavsky, A.M., Aguilar-Gaxiola, S., Alhamzawi, A.O., Alonso, J., Angermeyer, M., Benjet, C., Bromet, E., Chatterji, S., de Girolamo, G., Demyttenaere, K., Fayyad, J., Florescu, S., Gal, G., Gureje, O., Haro, J.M., Hu, C.Y., Karam, E.G., Kawakami, N., Lee, S., Lepine, J.P., Ormel, J., Posada-Villa, J., Sagar, R., Tsang, A., Ustun, T.B., Vassilev, S., Viana, M.C., Williams, D.R., 2010. Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *Br. J. Psychiatry* 197 (5), 378–385.
- Koenig, M.A., D'Souza, S., 1986. Sex differences in childhood mortality in rural Bangladesh. *Soc. Sci. Med.* 22 (1), 15–22.
- Kraemer, S., 2000. The fragile male. *BMJ* 321 (7276), 1609–1612.
- Lee, S., Guo, W.J., Tsang, A., He, Y.L., Huang, Y.Q., Zhang, M.Y., Liu, Z.R., Shen, Y.C., Kessler, R.C., 2011. The prevalence of family childhood adversities and their association with first onset of DSM-IV disorders in metropolitan China. *Psychol. Med.* 41 (1), 85–96.
- Lee, S., Tsang, A., Von Korff, M., de Graaf, R., Benjet, C., Haro, J.M., Angermeyer, M., Demyttenaere, K., de Girolamo, G., Gasquet, I., Merikangas, K., Posada-Villa, J., Takeshima, T., Kessler, R.C., 2009. Association of headache with childhood adversity and mental disorder: cross-national study. *Br. J. Psychiatry* 194 (2), 111–116.
- Levine, S.Z., Leucht, S., 2016. Identifying a system of predominant negative symptoms: network analysis of three randomized clinical trials. *Schizophr. Res.* 178 (1–3), 17–22.
- Levine, S.Z., Levav, I., Yoffe, R., Becher, Y., Pugachova, I., 2016. Genocide exposure and subsequent suicide risk: a population-based study. *PLoS One* 11 (2), e0149524.
- Madhoo, M., Levine, S.Z., 2016. Network analysis of the quick inventory of depressive symptomatology: reanalysis of the STAR*D clinical trial. *Eur. Neuropsychopharmacol.* 26 (11), 1768–1774.
- McGavock, L., Spratt, T., 2017. Children exposed to domestic violence: using adverse childhood experience scores to inform service response. *Br. J. Soc. Work* 47 (4), 1128–1146.
- McLaughlin, K.A., Green, J.G., Gruber, M.J., Sampson, N.A., Zaslavsky, A.M., Kessler, R.C., 2010. Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication II: associations with persistence of DSM-IV disorders. *Arch. Gen. Psychiatry* 67 (2), 124–132.
- McNally, R.J., 2016. Can network analysis transform psychopathology? *Behav. Res. Ther.* 86, 95–104.
- Mendenhall, E., 2017. Syndemics: a new path for global health research. *Lancet* 389 (10072), 889–891.
- Mendenhall, E., Kohrt, B.A., Norris, S.A., Ndeti, D., Prabhakaran, D., 2017. Non-communicable disease syndemics: poverty, depression, and diabetes among low-income populations. *Lancet* 389 (10072), 951–963.
- Molnar, B.E., Buka, S.L., Kessler, R.C., 2001. Child sexual abuse and subsequent psychopathology: results from the National Comorbidity Survey. *Am. J. Public Health* 91 (5), 753–760.
- Morgan, C., Gayer-Anderson, C., 2016. Childhood adversities and psychosis: evidence, challenges, implications. *World Psychiatry* 15 (2), 93–102.
- Moyer, V.A., United States Preventive Services Task Force, 2013. Primary care interventions to prevent child maltreatment: U.S. preventive services task force recommendation statement. *Ann. Intern. Med.* 159 (4), 289–295.
- Nolen-Hoeksema, S., Girgus, J.S., 1994. The emergence of gender differences in depression during adolescence. *Psychol. Bull.* 115 (3), 424–443.
- Opsahl, T., Agneessens, F., Skvoretz, J., 2010. Node centrality in weighted networks: generalizing degree and shortest paths. *Soc. Netw.* 32, 245–251.

- Portwood, S.G., Lambert, R.G., Abrams, L.P., Nelson, E.B., 2011. An evaluation of the Adults and Children Together (ACT) Against Violence Parents Raising Safe Kids program. *J. Prim. Prev.* 32, 147–160.
- Pridemore, W.A., Damphousse, K.R., Moore, R.K., 2005. Obtaining sensitive information from a wary population: a comparison of telephone and face-to-face surveys of welfare recipients in the United States. *Soc. Sci. Med.* 61 (5), 976–984.
- Rasch, G., 1980. *Probabilistic Models for Some Intelligence and Attainment Tests*. The University of Chicago Press, Chicago.
- Rehan, W., Antfolk, J., Johansson, A., Jern, P., Santtila, P., 2017. Experiences of severe childhood maltreatment, depression, anxiety and alcohol abuse among adults in Finland. *PLoS One* 12 (5), e0177252.
- RTI, 2002. *Sudaan Release 8.0.1*. Research Triangle Institute, North Carolina.
- Sheikh, M.A., 2018a. Childhood adversities and chronic conditions: examination of mediators, recall bias and age at diagnosis. *Int. J. Public Health* 63 (2), 181–192.
- Sheikh, M.A., 2018b. Psychological abuse, substance abuse distress, dissatisfaction with friendships, and incident psychiatric problems. *J. Psychosom. Res.* 108, 78–84.
- Sheikh, M.A., Abelsen, B., Olsen, J.A., 2016a. Clarifying associations between childhood adversity, social support, behavioral factors, and mental health, health, and well-being in adulthood: a population-based study. *Front. Psychol.* 7, 727.
- Sheikh, M.A., Abelsen, B., Olsen, J.A., 2016b. Differential recall bias, intermediate confounding, and mediation analysis in life course epidemiology: an analytic framework with empirical example. *Front. Psychol.* 7, 1828.
- Simon, G.E., VonKorff, M., 1995. Recall of psychiatric history in cross-sectional surveys: implications for epidemiologic research. *Epidemiol. Rev.* 17 (1), 221–227.
- Singer, M., 2000. A dose of drugs, a touch of violence, a case of AIDS: conceptualizing the SAVA syndemic. *Free Inq. Creat. Sociol.* 28 (1), 13–24.
- Singer, M., Bulled, N., Ostrach, B., Mendenhall, E., 2017. Syndemics and the biosocial conception of health. *Lancet* 389 (10072), 941–950.
- Straus, M.A., 1979. Measuring intrafamily conflict and violence: the conflict tactics (CT) scales. *J. Marriage Fam.* 41 (1), 75–88.
- Teicher, M.H., Samson, J.A., Polcari, A., McGrenery, C.E., 2006. Sticks, stones, and hurtful words: relative effects of various forms of childhood maltreatment. *Am. J. Psychiatry* 163 (6), 993–1000.
- Tibshirani, R., 1996. Regression shrinkage and selection via the lasso. *J. R. Stat. Soc. Ser. B* (58), 267–288.
- Tronick, E., Reck, C., 2009. Infants of depressed mothers. *Harv. Rev. Psychiatry* 17 (2), 147–156.
- Van Borkulo, C.D., 2015. **Network Comparison Test: permutation-based test of differences in strength of networks.** <https://github.com/cvborkulo/NetworkComparisonTest>. Accessed March 5, 2018.
- van Borkulo, C.D., Borsboom, D., Epskamp, S., Blanken, T.F., Boschloo, L., Schoevers, R.A., Waldorp, L.J., 2014. A new method for constructing networks from binary data. *Sci. Rep.* 4, 5918.
- Viana, M.C., Teixeira, M.G., Beraldi, F., Bassani Ide, S., Andrade, L.H., 2009. Sao Paulo Megacity Mental Health Survey—a population-based epidemiological study of psychiatric morbidity in the Sao Paulo metropolitan area: aims, design and field implementation. *Rev. Bras. Psiquiatr.* 31 (4), 375–386.
- Viana, M.C., Viana-Moldes, I., Teixeira, M., Basani, I., Andrade, L.H., 2004. *The World Mental Health Survey Initiative Version of the Composite International Diagnostic Interview (WMH-CIDI): translation and adaptation to Brazilian-Portuguese: the instrument used in the “São Paulo Megacity Mental Health Survey”*. Printed version.
- Weinstein, Y., Levav, I., Gelkopf, M., Roe, D., Yoffe, R., Pugachova, I., Levine, S.Z., 2018. Association of maternal exposure to terror attacks during pregnancy and the risk of schizophrenia in the offspring: a population-based study. *Schizophr. Res.* 199, 163–167.
- Zanatta, L.F., Grein, M.I., Alvarez-Dardet, C., Moraes, S.P., Bretas, J.R., Ruiz-Cantero, M.T., Roses, M., 2016. Gender equality: why is Brazil moving backwards. *Cad. Saude Publica* 32 (8), e00089616.