



Depression and treatment outcome in anorexia nervosa

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ABSTRACT

Aim of this study was to compare the immediate and long-term effect of a cognitive-behavior therapy program for anorexia nervosa inpatients with and without concomitant Major Depressive Episodes (MDE). The program has been adapted from the “enhanced” form of Cognitive Behavior Therapy (CBT) for eating disorders. Sixty-three consecutive underweight adult patients with severe eating disorder were treated with inpatient CBT. MDE was assessed with the structured clinical interview for DSM-IV. The Eating Disorder Examination, and the Brief Symptom Inventory were recorded at entry, at the end of treatment, and 6- and 12-month later. MDE was present in 60.3% of participants. No significant differences were observed in the demographic and baseline clinical variables between patients with and without MDE. Significant improvements in weight, and in eating disorder and general psychopathology were showed. There were no differences between participants with and without MDE in terms of treatment outcome, and the severity of depression was not associated with changes in global Eating Disorder Examination score.

These findings suggest that a diagnosis of MDE does not influence the outcome of inpatient treatment for anorexia nervosa patients, and that the severity of depression cannot be used to predict the success or failure of such treatment.

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1. Introduction

Anorexia nervosa has high rates of co-morbidity with other psychiatric disorders, especially major depressive disorder. Indeed, several studies have found that major depressive disorder is the most common co-morbid diagnosis in these patients (Herzog et al., 1992; Kaye, 2008), with lifetime rates ranging between 50% and 75% (American Psychiatric Association, 2006). In the existing literature, clinical depression has been linked with worse anorexia nervosa outcome (Lowe et al., 2001), higher rates of suicide attempt (Bulik et al., 2008; Franko et al., 2004) and suicide-related mortality (Crow et al., 2009). However, hard data on the role of clinical depression in anorexia nervosa treatment outcome is scarce, and a general consensus still appears remote. For instance, while a few studies have found that pretreatment depression is predictive of poor immediate or long-term outcome of cognitive behavior therapy in patients with bulimia nervosa (Agras et al., 2000; Bossert et al., 1992; Bulik et al., 1998) no such link has been found in anorexia nervosa patients (Collin et al., 2010; Herpertz-Dahlmann et al., 1995).

Clinical trials evaluating antidepressant efficacy in the treatment of eating disorders found that antidepressants reduced

significantly the number of binge eating and self-induced vomiting episodes in bulimia nervosa and in binge eating disorder participants regardless the presence of comorbid depression (Goldstein et al., 1999). However, in another study on binge eating disorder participants, cognitive behavior therapy produced a significant higher reduction of depression and overevaluation of shape and weight than antidepressants (Grilo et al., 2012). Finally, antidepressants have not been associated with major depressive disorder recovery in anorexia nervosa participants (Mischoulon et al., 2010).

Despite the paucity of evidence, NICE guidelines, erring on the side of caution, list severe depression as one of the contraindications for eating disorder treatment, and recommend that such treatment be postponed until the depression has been dealt with (National Institute of Clinical Excellence, 2004). Cognitive behavioral theorists are also of the opinion that clinical depression should be treated with full-dose antidepressants prior to launching the psychological treatment (Fairburn et al., 2008).

However, some clinicians have suggested that it is, instead, preferable to focus initially on the treatment of eating disorders, the goal being to normalize weight and food intake before assessing and prescribing any treatment for co-existing psychiatric disorders (Garner, 1993; Mattar et al., 2012). The rationale behind this recommendation is based on the observation that many of the symptoms postulated to be a sign of psychiatric co-morbidity, including clinical depression, may actually result from low body

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weight and calorie restriction (American Psychiatric Association, 2006).

In order to shed some light on the issue, we set out to investigate the prevalence and associated features of ongoing clinical depression in a large group of inpatients with eating disorders, and to assess whether it influences treatment outcome.

2. Methods

2.1. Design

The study was conducted at an inpatient eating disorder unit. Consecutive eligible patients were treated with inpatient Cognitive Behavioral Therapy (CBT). Patients were assessed before treatment, after the end of treatment, and at 6- and 12-month follow-up. The period of hospitalization lasted 20 weeks, in which the treatment was administered in an inpatient setting for the first 13 weeks and in day hospital for the remaining seven. The ethical committee of the Local Health Unit 22-Bussolengo approved the study, and all participants gave informed written consent to their participation and to the anonymous use of their personal data.

2.2. Participants

The sample consisted of 63 adult anorexia nervosa patients consecutively admitted to the inpatient eating disorder unit of Villa Garda Hospital (Northern Italy). The patients were referred from all over Italy by general practitioners or outpatient eating disorder specialists. For admission, patients had to be aged between 18 and 65 years, to fulfill the DSM-IV diagnostic criteria for anorexia nervosa (American Psychiatric Association, 2006) bar the amenorrhea criterion, as judged by both the referring clinician and an in-house eating disorder specialist (RDG), and to require inpatient treatment either as a result of failure of outpatient treatment or because the eating disorder could not be managed safely on an outpatient basis.

Eighty percent (63/79) of eligible patients agreed to undergo the treatment, and were added to the unit's waiting list. During the waiting period, which lasted up to eight weeks, the patients were managed by their referring clinician. Four percent (3/79) of the eligible patients were excluded from the study for the following reasons (acute psychotic state, $N=1$; significant substance abuse, $N=2$), while 16% (13/79) declined to participate. Fig. 1 shows the recruitment and retention figures for the participants.

2.3. Inpatient treatment protocol

The treatment adopted as standard in the unit has been adapted from the "enhanced" form of CBT for eating disorders (Fairburn, 2008) to make it suitable for an inpatient setting. The program retains all the main strategies and procedures of enhanced CBT, which were delivered in both individual and group sessions. However, the program differs from outpatient enhanced CBT in that meals are assisted by dietitians in the early weeks of hospitalization. Details of the program are provided elsewhere (Dalle Grave, 2012; Dalle Grave et al., 2008).

Psychotropic medications were not prescribed during the treatment, and the psychotropic drugs being taken by patients at admission were gradually phased out during the first 2 weeks of hospitalization, while patients were under the supervision of clinic staff.

2.4. Assessment and measures

2.4.1. Demographic and clinical variables

Demographic and clinical variables were obtained in the course of a direct interview. Weight (to the nearest 0.1 kg) was measured on calibrated scales, and height (to the nearest 0.5 cm) using a stadiometer. Patients were weighed and measured in their underwear, without shoes.

2.4.2. Eating disorder features

These were assessed using the validated Italian version of the 12th edition of the Eating Disorder Examination interview (Fairburn and Cooper, 1993; Mannucci et al., 1997). The Eating Disorder Examination was administered by assessors who were trained and supervised by RDG, an expert in the use of the tool. The assessors had no involvement in the treatment itself.

2.4.3. General psychopathological features

These were measured using the validated Italian version of the Brief Symptom Inventory (De Leo et al., 1993; Derogatis and Melisaratos, 1983) a short version of the Symptom Checklist-90 (Derogatis and Cleary, 1977). The Brief Symptom Inventory includes three scales designed to measure global psychological distress

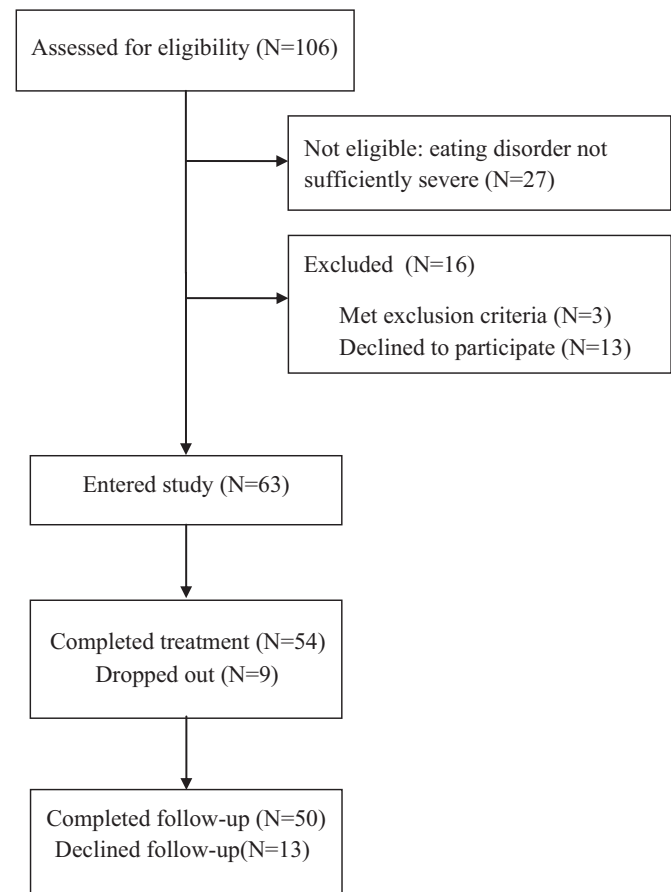


Fig. 1. Consort diagram.

and nine, more specific, subscales. For the purpose of our study we used the Global Severity Index (GSI) and the Depression subscale. The Structured Clinical Interview for DSM-IV (First et al., 1995) was used at baseline to identify the presence of coexisting axis I psychiatric disorders.

2.5. Statistical analyses

Continuous variables were categorized as means (S.D.) or medians (interquartile range), and categorical variables as frequencies and percentages. The significance of differences between the groups at baseline was calculated by means of the *T*-test or chi-squared test or Fisher's Exact test, as appropriate.

To assess the different effects of inpatient enhanced CBT intervention on each outcome (body weight, body mass index, Eating Disorder Examination global and subscale scores, Brief Symptom Inventory global and depression scores) at the end of therapy and at 6- and 12-month follow-up in participants with Major Depressive Episodes (MDE) and without (no-MDE), we used linear mixed model that included all four time-point outcome as dependent variables. Fixed parts of the model included a dummy variable indicating MDE and no-MDE groups, to account for the differences between the two groups, and the two groups (MDE vs. no-MDE) $\times$ time interaction, to evaluate different changes in the two groups over time. As covariates we included the baseline measure of the outcome. Mixed effect models have been endorsed as a rigorous method of analyzing longitudinal repeated-measures data from therapy studies (Houck et al., 2004). Moreover, when the missing data is ignorable, and the model describing individual growth patterns is correctly specified, the mixed effect model provides valid inferences in the presence of missing data (Laird, 1988). These models can be applied to both normally distributed continuous outcomes as well as categorical outcomes and other non-normally distributed outcomes, and allow us to analyze data under general assumptions regarding the missing data (i.e., missing at random) (Gibbons et al., 2010). We found evidence to support the missing-at-random assumption in the present data. We assessed a number of baseline variables (age, occupation, length of illness duration) for their ability to predict missingness at each time point measured by a categorical variable (missing data at that time point for that participant Yes/No) using logistic regression. These variables, and their interactions with time, did not predict changes in any of our dependent variables, suggesting that missing data did not influence outcomes. We therefore analyzed the effect of

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