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Research report

Impact of bariatric surgery on clinical depression. Interrupted time series study with matched controls

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ABSTRACT

Background: Obesity is associated with depression. This study aimed to evaluate whether clinical depression is reduced after bariatric surgery (BS).
Methods: Obese adults who received BS procedures from 2002 to 2014 were sampled from the UK Clinical Practice Research Datalink. An interrupted time series design, with matched controls, was conducted from three years before, to a maximum of seven years after surgery. Controls were matched for body mass index (BMI), age, gender and year of procedure. Clinical depression was defined as a medical diagnosis recorded in year, or an antidepressant prescribed in year to a participant ever diagnosed with depression. Adjusted odds ratios (AOR) were estimated.
Results: There were 3045 participants (mean age 45.9; mean BMI 44.0 kg/m^2) who received BS, including laparoscopic gastric banding in 1297 (43%), gastric bypass in 1265 (42%), sleeve gastrectomy in 477 (16%) and six undefined. Before surgery, 36% of BS participants, and 21% of controls, had clinical depression; between-group AOR, 2.02, 95%CI 1.75–2.33, $P<0.001$. In the second post-operative year 32% had depression; AOR, compared to time without surgery, 0.83 (0.76–0.90, $P<0.001$). By the seventh year, the prevalence of depression increased to 37%; AOR 0.99 (0.76–1.29, $P=0.959$).
Limitations: Despite matching there were differences in depression between BS and control patients, representing the highly selective nature of BS.
Conclusions: Depression is frequent among individuals selected to undergo bariatric surgery. Bariatric surgery may be associated with a modest reduction in clinical depression over the initial post-operative years but this is not maintained.

1. Introduction

The relationship between obesity and depression is complex. Obese people are at higher risk of depression but depression is also a predictor of weight gain and future obesity (Luppino et al., 2010). People who are obese experience the onset of morbidity at younger ages than those with lower body weight (Booth et al., 2014) and the multiple morbidities associated with obesity may contribute to a higher prevalence of depression (Bhattarai et al., 2013). Bariatric surgery is an increasingly accepted treatment option in obese patients being recommended for those with morbid obesity (body mass index, BMI ≥ 40 kg/m^2), as well as those with severe obesity (BMI ≥ 35 kg/m^2) if there are weight-related co-morbidities not responding to medical management (National Institute for Health and Clinical Excellence, 2006). Access to bariatric surgery is presently limited, patients undergoing bariatric surgery for obesity represent a highly selected group, often with a high prevalence of clinical depression (Kalarchian et al., 2007, Sarwer et al., 2004).

There is now increasing evidence from randomised controlled trials that bariatric surgery is associated with substantial weight loss and remission of diabetes (Gloy et al., 2013) with evidence of wider benefits suggested by non-randomised studies with long-term follow-up (Arterburn and Courcoulas, 2014). However, evidence for an effect of BS on depression is limited. Several longitudinal studies have explored the relationship between bariatric surgery and depression, identifying significant reductions in depression (Burgmer et al., 2007)

Abbreviations: AOR, Adjusted odds ratio; BS, Bariatric surgery; BMI, Body mass index; CPRD, Clinical Practice Research Database; CHD, Coronary heart disease; LAGB, Laparoscopic adjustable gastric banding; WHO, World Health Organisation

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and depressive symptoms (Dixon et al., 2003, Mitchell et al., 2014) following surgery. One study found a decrease in depression from 32.7% at baseline, to 16.5% at 6–12 months, and 14.3% at 2–3 years following surgery (de Zwaan et al., 2011). However, other studies suggest that improvements following surgery may not be maintained after the first post-operative year (Mitchell et al., 2014) and depressive symptoms may deteriorate in some patients (Ivezaj and Grilo, 2014). Previous reports have often drawn on data from hospital-based series that did not include control groups, often with short durations of follow-up. The present study aimed to evaluate whether bariatric surgery is associated with a reduction in clinical depression up to a maximum of seven years following the procedure. A population-based cohort provided the data source for an interrupted time-series design with matched controls, facilitating a pragmatic evaluation of the impact of BS on clinical depression recorded in primary care electronic health records.

2. Methods

2.1. Study design and participants

A controlled interrupted time-series study was conducted, drawing on data for obese participants who received bariatric surgery and matched obese control participants who did not receive surgery, by evaluating multiple time points both before and after the bariatric surgical procedure. Electronic health records from primary care were evaluated for clinical diagnoses of depression and prescription of anti-depressant drugs in the three years before-, and seven years after-, bariatric surgery.

Participants were selected from the UK Clinical Practice Research Datalink (CPRD). The CPRD is a prospectively collected database of research-quality primary care electronic health records including demographic, clinical, diagnostic and prescribing information for approximately 6% of the UK population (Herrett et al., 2010, Williams et al., 2012). Ethical approval for the study was given by the CPRD Independent Scientific Advisory Committee (ISAC 13_089).

All participants with a record of bariatric surgery from 1st January 2000 to the 30th April 2012 were sampled, including laparoscopic adjustable gastric banding (LAGB), gastric bypass and sleeve gastrectomy. The first date on which surgery was recorded was taken as the index date. The earliest index event was in 2002. Participants aged less than 20 years or without a BMI record indicating obesity (BMI $\geq$ 30 kg/m^2) prior to surgery were excluded. Participants with BS recorded less than 12 months after the start of their record were also excluded, because these records might have referred to BS procedures performed before the participant joined the general practice.

BS participants were individually matched with a cohort of control participants, matched for gender, age, BMI and index year. The index date for control participants was the date on which they first entered their highest BMI category. All controls had a minimum of 12 months record before the index date. Nearest neighbour matching was used to select the control cohort.

2.2. Outcomes and covariates

Clinical depression was identified through medical diagnoses for depression recorded in clinical or referral records as well as through prescriptions for anti-depressant drugs. Participant records were divided into person-years before- and after-surgery. Individuals were classified as having clinical depression in a given person-year if they had a medical diagnosis of depression recorded in that year, or if they were prescribed antidepressant drugs in the year and were ever diagnosed with depression (Bhattarai et al., 2013). BMI was categorised using the World Health Organisation (WHO) criteria using the most recent record prior to the index date. Co-morbidities were evaluated including stroke, coronary heart disease (CHD) and type 2 diabetes. Records for hypertension (blood pressure $\geq$ 140/90 mm Hg), high cholesterol (total cholesterol $\geq$ 5 mmol/L) and current smoking status were evaluated. Participants were also classified according to whether they were treated with anti-hypertensive or lipid-lowering medications.

2.3. Analysis

Baseline characteristics in the surgery and control groups were compared. Participant records were divided into one year periods from up to three years before, to a maximum of seven years after, the index date. The presence or absence of clinical depression was evaluated for each one year period. A multiple logistic regression analysis was conducted using person years as observations and the presence or absence of clinical depression in each year as the outcome. A model was fitted to evaluate the effect of group (BS or control); study year from three years before to seven years after surgery; and time after surgery, included, for improved goodness-of-fit, as indicator variables for each post-operative year (Penfold and Zhang, 2013). The reference category was all person-time without surgery from the control group and the bariatric surgery group before operation. The model was adjusted for gender, age, baseline BMI, index year, type of BS procedure, prevalent diabetes mellitus, coronary heart disease and stroke, smoking status, high blood pressure and cholesterol, and treatment with anti-hypertensive or lipid-lowering drugs. Robust variance estimates were employed to adjust standard errors for clustering of person years by participant.

3. Results

There were 4793 participants with bariatric surgery recorded; 1324 participants with bariatric surgery first recorded less than one year after the start of the patient record were excluded, as were 14 participants aged less than 20 years at the index date, and 401 participants with either no BMI record before surgery or BMI values less than 30 kg/m^2 prior to surgery. Nine participants with a record of gastric band removal before the index date were also excluded. There were then 3045 participants identified as having bariatric surgery for obesity and 3045 matched controls. BS procedures included laparoscopic gastric banding (LAGB) in 1297 (43%), gastric bypass in 1265 (42%), sleeve gastrectomy in 477 (16%) and six undefined type. Utilisation of BS increased over the period and LAGB accounted for 97% of 104 procedures before 2006, but only 20% of 924 procedures from 2012 onwards, with increasing use of gastric bypass and sleeve gastrectomy. The median year of procedure was 2010, consequently only a minority of participants contributed more than three years of follow-up data.

Characteristics of the surgery and control participants at the index date are presented in Table 1. The majority of surgical procedures were conducted in women (79%) and in participants with morbid obesity (65%). The mean age at surgery was 45.9 years. Participants undergoing bariatric surgery more frequently had type 2 diabetes (29% vs. 14%, $P < 0.001$), hypercholesterolaemia (35% vs. 25%, $P = 0.022$) and were more likely to be prescribed anti-hypertensive drugs and statins than controls.

Table 2 shows the number of participants analysed by year before and after surgery. There were 63% contributing to follow-up after the end of two years and 31% in the fifth year of follow-up. In the year prior to surgery, 36% of surgery participants met the criteria for prevalent clinical depression in comparison to 21% of control participants (Fig. 1 and Table 2). In the two years following surgery, this reduced to 32% in the participants who underwent surgery before rising to pre-surgery levels (37%) in the seventh year