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RESEARCH ARTICLE

Influence of Obesity in Mortality in Hospitalized Adults with Type 2 Diabetes

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Abstract

Background: The aim of the present study is to assess the association between obesity and mortality in hospitalized patients with type 2 Diabetes Mellitus (T2DM) as well as the risk of readmission in less than 30 days.

Methods: A retrospective chart review of a cohort of consecutive patients admitted with T2DM in internal medicine wards in Spain between January 1st, 2005, and December 31st, 2013, was performed. Patients with a diagnosis of obesity were identified. The mortality and re-admittance indexes of obese patients were compared with the subpopulation without theses diagnosis.

Results: A total of 1,499,282 admittances were analyzed and 199,871 (13.3%) diagnosis of obesity were identified. Obese patients showed a lower in-hospital mortality risk (odds ratio [OR], 0.667; 95% confidence interval [CI], 0.647-0.675) and early re-admittance risk (OR, 0.96; 95% CI, 0.94-0.97) than the non-obese even after adjusting for possible confounding factors.

Conclusions: Obesity in those hospitalized for T2DM in internal medicine wards is associated with reduced in-hospital mortality risk, early re-admittance and shorter length of stay.

Introduction

Overweight and obesity increase overall mortality and predict premature death (7-10). Furthermore, obesity is associated with the development of cardiovascular risk factors like increased insulin resistance and type 2 diabetes mellitus (T2DM), hypertension and dyslipidemia [1-3].

The association between obesity and increased risk for cardiovascular disease (CVD) is well-established in the general population [4,5]. Paradoxically, once CVD occurs, obesity seems to confer a survival advantage. There is growing evidence that overweight patients with CVD survive longer than their normal weight counterparts, an effect called the "obesity paradox".

Nevertheless, in a range of cardiovascular conditions such as heart failure [6,7], stroke [8,9], coronary heart disease survivors [10], as well as patients in chronic hemodialysis [11], renal failure [12], chronic obstructive pulmonary disease (COPD) [13,14], cancer [15] and rheumatoid arthritis [16], an "obesity paradox "has been raised. Specifically, the prognosis of overweight and obese individuals seemed to be better than the prognosis of normal or low-weight subjects.

A similar obesity paradox might exist after type 2 diabetes has developed. In two contemporary studies, the Translating Research Into Action for Diabetes (TRIAD) study [17] and the Proactive trial [18] participants with diabetes who were normal weight at the baseline examination or who lost weight during the trial (PROactive) experienced higher mortality than participants who were overweight or obese.

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Different studies have been published investigating the relationship between obesity (mostly defined by BMI) and mortality in type 2 diabetes. The results are inconsistent and contradictory. The majority of them reported an increase in mortality in obese patients with type 2 diabetes, with a U-shaped relationship (increased risk at lower and higher BMIs) [19-26]. In contrast, other studies showed that being overweight or obese was associated with better overall survival rates [17,27-29]. All these studies investigated the relationship between obesity and mortality in the follow up of type 2 diabetes mellitus patients.

However, few studies have analyzed the effect of obesity in in-hospital outcomes. While higher BMI may confer an advantage against mortality in the critical patient [30] and medical inpatients [31], in surgical populations mixed results have been reported [32,33].

Specifically, it is not well known if obesity modifies the in-hospital prognosis of diabetic patients. A recent study [34] has explored the impact of BMI and hyperglycemia on mortality and complications in hospitalized patients without showing the presence of an obesity paradox among diabetic inpatients.

The present study aims to investigate the association between obesity and mortality in medical patients hospitalized with T2DM, the length of stay and the risk of readmission in the next 30 days after discharge. The use of a large contemporary database has allowed closer examination of any graded association between obesity and mortality than among smaller studies.

Methods

We identified every patient discharged from Internal Medicine Departments among hospitals of the Spanish Public Health Service between January 1st, 2005 and December 31st, 2013. Hospitals discharge data were obtained from the BMDS (Basic Minimum Data Set). BMDS contains socio-demographic and clinical data for each documented hospital admission including: gender and age, primary and secondary diagnoses (according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code); primary and secondary procedures; admission and discharge status; length of stay, and hospital characteristics (group 1: less than 150 beds; group 2: 150 to 200 beds; group 3: 200 to 500 beds; group 4: 500 to 1,000 beds; group 5: more than 1,000 beds). For every patient, a diagnosis-related group (DRG) was identified. DRGs are a method of classifying patient hospitalizations by diagnosis and procedures on the assumption that similar costs are expended on patients by using similar resources. The CMBD registry is compulsory for every patient admitted to a hospital of the Spanish National Health Service, a system that cares for more than 90% of the country's population.

Cases were selected if they had a diagnosis of diabetes. The diagnosis of diabetes was identified using ICD-9-MC codes 250.00-250.99 in the diagnosis field. Patients who had a secondary diagnosis of obesity (ICD-9-CM: 278.00-278.02) were analyzed.

The standardized definition of the variable readmission in the Spanish CMBD has been defined as a new hospitalization in the following month with the same Major Diagnostic Category in the main diagnosis.

The Age Adjusted Charlson Co-morbidity Index (CCI) was computed for each patient. This index reflects the number and importance of comorbid diseases, relies on ICD-9-CM categories, and was used to adequately adjust for severity of illness [35,36].

The following risk factors were identified using ICD-9-MC codes in any primary or secondary diagnosis field: Tobacco: ICD-9-CM 305.10, Hypertension: ICD-9-CM 401.0, 401.1, 401.9, Acute myocardial infarct: ICD-9-CM 410.xx, 412, Heart failure: ICD-9-CM 398.91, 404*, 402.11, 402.91, 428-428.9, Cerebrovascular disease: ICD-9-MC 430.00-438.99, COPD: ICD-9-CM 416.8, 416.9, 500-505, 490-496, Liver disease: ICD-9-CM 571.0-571.99, Diabetes decompensation: ICD-9-CM 250.32, 250.33, 250.42, 250.43, 250.52, 250.53, 250.62, 250.63, 250.72, 250.73, 250.82, 250.82, 250.92, 250.93, Kidney Chronic disease: ICD-9-CM 585.00-586.99, 582.00-582.9, 583.00-583.7, 588.0-588.9, Neoplasia: ICD-9-CM 140.0-172.9, 174.0-195.8, 200-208.9, Malnutrition: ICD-9-CM 260-263.9, Pressure ulcer: ICD-9-CM 707.xx, Urinary tract infection: ICD-9-CM 599.00, 590.xx, 646.60-49, 601.

Data Analysis

A descriptive analysis of these patients was carried out, and the demographic variables among the patients diagnosed with or without obesity were compared. We used the chi-square test for categorical variables with the Yates correction, the Fisher's exact test for dichotomous variables when the expected value of a cell was less than 5, and Student's t-test or ANOVA for quantitative variables. All the univariate analyses were carried out after adjusting for age and gender. The Odds-Ratios (OR) and 95% Confidence Intervals (CI) were estimated from the regression coefficients.

As this is an administrative database, the control of the confounding variables is basic. For this reason, a multivariate logistic regression analysis was carried out with the aim of determining the excess of mortality attributable to obesity, after the correction of possible confounding variables such as the age of the patient (in years, as a continuous variable), Charlson index (in points, as a continuous variable), sex and all variables that had demonstrated a statistically significant relation in the univariate analysis with mortality and are no included in the Charlson index. A logistic regression analysis with backward stepwise procedure and p > 0.10 as the criterion for exclusion, was used to find the best predictive models. Stratified analyses were performed to examine confounders and interactions were appropriate. All statistical analyses were carried out with the use of a SPSS Software version 16 (Chicago, Illinois, SPSS Inc).

Results

We identified 1,499,252 discharges with T2DM diagnosis during the study period. A total of 199,871 (13.3%) subjects were obese. The main characteristics in obese and non-obese patients of our series are listed in Table 1. Compared with non-obese, obese patients were more frequently women (62.6% versus 47.8% P.001), younger (71.87 versus 76.33 P.001), more frequently smokers (9.1% versus 7.3% P.001).

Comorbid conditions were common and are listed in Table 1. Obese patients had more frequently hypertension, heart failure, chronic obstructive pulmonary disease, diabetes decompensation and kidney chronic disease. Non obese had more frequently acute myocardial infarction, dementia, cerebrovascular disease, liver disease, neoplasia, and malnutrition, pressure ulcers, urinary tract infection, Charlson > 2, in-hospital mortality, longer admission stay and readmission < 30 days.

A multivariable logistic regression analysis was performed showing that obese patients had a 34% lower risk of mortality than non-obese patients, after adjusting for potential confounding factors (OR, 0.667; 95% CI, 0.647-0.675 (Table 2). In addition, the risk of readmission was linked to increasing age, CCI, and gender, and obese patients were less likely to be readmitted (OR, 0.96; 95% CI, 0.94-0.97; Table 2).

Discussion

The present study shows that obese T2DM patients had a significantly lower mortality during hospitalization and a lower risk of readmission in the next 30 days after discharge. The risk of mortality is lower in obese patients by 34% and of readmission at 30 days by 4%. Length of stay was also shorter in obese T2DM patients than in non-obese (9.15 days vs. 9.66; p < 0,001).

Our study includes a great number of patients

Table 1: Risk factors and baseline characteristics of 1,499,282 type 2 diabetes mellitus patients according to obesity or non obesity.

Characteristics	Obese (199,871)	Non obese (1,299,411)	P value
Age, mean (SD) yr	71,87 (11.4)	76,33 (11.7)	< 0.001
Gender (female)	125,155 (62.6%)	621,314 (47.8%)	< 0.001
Smoking	18,120 (9.1%)	95,506 (7.3%)	< 0.001
Hypertension	125,102 (62.6%)	740,589 (57%)	< 0.001
Acute myocardial infarction	9,329 (4.7%)	69,149 (5.35)	< 0.001
Heart failure	42,332 (21.2%)	198,736 (15.3%)	< 0.001
Dementia	3,654 (1.8%)	69,726 (5.4%)	< 0.001
Cerebrovascular disease	13,224 (6.6%)	130,493 (10.0%)	< 0.001
COPD	56,100 (28.1%)	294,298 (22.6%)	< 0.001
Liver disease	3,061 (1.5%)	37,250 (2.9%)	< 0.001
Diabetic decompensation	22,967 (11.5%)	122,194 (9.4%)	< 0.001
Kidney chronic disease	34,116 (17.1%)	217,663 (16.8%)	< 0.001
Neoplasia	6,028 (3.0%)	78,163 (6.0%)	< 0.001
Malnutrition	1,161 (0.6%)	22,624 (1.7%)	< 0.001
Pressure ulcer	2,497 (1.2%)	38,667 (3.0%)	< 0.001
Urinary tract infection	18,984 (9.5%)	166,890 (12.8%)	< 0.001
Charlson > 2	64,843 (32.4%)	462,282 (35.6%)	< 0.001
Mortality	10,916 (5.5%)	133,251 (10.3%)	< 0.001
Length of stay, mean (SD), days	9,15 (8.5)	9,66 (10.2)	< 0.001
Readmission (< 30 days)	27,083 (14.6%)	191,131 (16%)	< 0.001

Table 2: Multivariate analysis evaluating the association between obesity and clinical outcomes.

Characteristics	OR	95% CI	P value
Inpatient mortality			
Age (10 yr)	1.058	1.057-1.059	< 0.001
Gender (female)	1.007	0.995-1.019	0.238
Charlson > 2	1.228	1.225-12231	< 0.001
Obesity	0.667	0.647-0.675	< 0.001
Readmission			
Age (10 yr)	1.064	1.060-1.068	< 0.001
Gender	0.927	0.918-0.936	< 0.001
Charlson > 2	1.136	1.133-1.139	< 0.001
Obesity	0.961	0.948-0.975	< 0.001

(1,499,252; all subjects admitted to internal medicine departments in Spain during 9 years with a diagnosis of T2DM). Among this population we identified 199,871 (13.3%) with a diagnosis of obesity.

Our findings are similar to other studies. Doehner, et al. [18] from the original PROactive study population, included 5,202 patients (99.3%) with enough weight measurements to be included in their analysis concluding that among patients with T2DM and cardiovascular co-morbidity, overweight and obese patients had a lower mortality compared to patients with normal weight. Weight loss but not weight gain was associated with increased mortality and morbidity.

Carnethon, et al. [27] in a longitudinal study, patients who had a normal weight at the time of incidental diabetes experienced higher total and non cardiovascular mortality as compared with those who were overweight or obese. Liu, et al. report in a recent work an association between body-mass index and mortality in Chinese adults with T2DM during a mean follow-up period of 7.25 ± 1.42-years. The risk for all-cause mortality was lower in the overweight and the obese groups than in those in the normal weight and the underweight groups [37].

Logue, et al. [25] using records of 106,640 patients in Scotland assessed and U-shaped relationship between BMI (Body Mass Index) within a year after diagnosis of diabetes and subsequent mortality, with BMI of 25 to < 30 kg/m^2 associated with the lowest mortality risk > 2 years after diagnosis of diabetes.

Costanzo, et al. [38] investigated the association between body weight and prognosis in a large cohort of 10,568 patients with T2DM with a long follow up (median of 10.6 years) and found that being overweight or obese was associated with higher risk of nonfatal cardiovascular events but not mortality. The BMI associate with best survival rated from the conventional normal (18.5 to 24.9 kg/m^2) to the overweight (25 to 29.9).

However, other studies do not reach the same conclusions. In a recent retrospective analysis Alexopoulos, et al. [34], investigated the impact of obesity in hospitalized patients with hyperglycemia and diabetes (72.8% did not have diabetes) and concluded that obesity was not associated with a higher morbidity or mortality in hospitalized patients when compared to normal weight regardless of glycemic status. No 'obesity paradox' was observed in the hospital setting among patients with diabetes and hyperglycemia. Ross, et al. [20] concluded that average body weight was associated with the best survival in their cohort of 373 patients (men and women), with a J-shaped relative risk curve and a poorer survival rate for those thin, overweight or obese. Mulnier, et al. [23] in a large cohort selected from the General Practice Research Database, of 44,230 patients with T2DM, the hazard ratio for all-cause mortality using BMI 20-24 kg/m^2 as the reference range, was 1.43 for those with BMI 35-54 kg/m^2.

Tobias, et al. [26] in a 11,427 participants study observed an a J-shaped association between BMI and all-cause mortality, those in the lowest BMI (18.5 to 22.4) had a significantly elevated mortality as did those in the highest categories (30-34.9); the lowest risk observed among the normal-weight (BMI 22.5 to 24.9).

The results are discordant even among the methodologically strongest reports, because in some of them the sample is small, smoking and hypertension are not recorded, comorbid conditions were not taken, in others underweight patients were classified as normal, etc.

Our study is the first one that analyses the influence of obesity during hospitalization in medical diabetic patients. The strengths of our work are the size of the sample, we recorded key characteristics as smoking and blood pressure, considered comorbid conditions and the information was gathered from an official data base that registers all the activity of internal medicine departments in Spain.

The reason for this ''obesity paradox'' in patients with T2DM is unclear. Our obese patients show a higher prevalence in the association of hypertension and smoking than the normal-weight population and are also younger. These circumstances could make them visit their physician earlier and be appropriately medicated for these diseases. Compared with normal-weight patients, overweight/obese patients have a better metabolic reservoir, an aspect that allows them to deal better with the systemic catabolic imbalance and impaired metabolic efficiency induced by the hospitalization [39].

Another possible explanation for the obesity paradox involves the role of adipose tissue in reducing systemic inflammation in these patients. It has been suggested that adipose tissue produces tumor necrosis factor-a (TNF-a) receptors, positively correlating with body fat levels, which act by neutralizing the harmful effects of TNF-a. Therefore, overweight and obese patients could benefit from the higher levels of these receptors, compared with normal-weight and underweight subjects [40]. An aspect to emphasize is that most studies assessing obesity and mortality have relied on BMI to define obesity. Body mass index as a measure of body composition, lacks the ability to quantify percent body fat and distinguish between lean and fat body mass. Furthermore, in diseased patients, BMI is not a sensitive marker of nutritional status, especially in patients with hyper-hydration and edema [41]. In our opinion, to establish a clear-cut relationship between obesity and cardiovascular-related mortality, other measures of obesity, especially those accounting for central obesity, such as waist circumference, waist-to-hip ratio, and waist-to-height ratio, which might be more accurate for cardiovascular risk stratification, should be used [9].

There is a well-established association found between obesity related DNA methylation patterns at birth and adult onset obesity and diabetes. Epigenetic markers may serve to screen individuals at risk for obesity and assess the effects of interventions in early life that may delay or prevent obesity early. This might contribute to lower the obesity-related burden of death and disability as a health measure [42].

Some potential limitations of the present study deserve comment. In our database obesity is recorded only as a diagnosis, we don't have BMI or any of the other measures of obesity. There has only been limited evaluation of how frequently obesity is actually captured in administrative databases or how accurately is captured. A recent study by Martin, et al. [43] to assess the validity of obesity coding in administrative database confirmed that obesity was poorly coded; however, when coded, it was coded accurately. Perhaps administrative databases are not an optimal data source for obesity prevalence but could be used to define obese cohorts especially in hospitalized patients. In conclusion, on the basis of the present study of patients with T2DM hospitalized in internal medicine wards in Spain trough a unique database from an integrated health-care system, we conclude that obesity appears to be associated with an important reduction in mortality during admissions and also with a reduction of readmission in the next 30 days and shorter length of stay.

The obesity paradox is a complex phenomenon that requires additional investigation and future studies should consider weight change when evaluating the longitudinal association among health, overweight/obesity, and outcomes. It is possible that other measures of obesity besides BMI should be needed.

Conflict of Interest

The authors state that they have no conflicts of interest.

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