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Original article

Changes in body mass index following newly diagnosed type 2 diabetes and risk of cardiovascular mortality: A cohort study of 8486 primary-care patients

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Abstract

Aims. – Elevated body mass index (BMI) is associated with an increased risk of type 2 diabetes and cardiovascular disease (CVD). This study explored the association between BMI changes in the first 18 months of newly diagnosed type 2 diabetes and the risk of long-term CVD mortality.

Methods. – A total of 8486 patients with newly diagnosed type 2 diabetes and no previous history of CVD or cancer were identified from 84 primary-care centres in Sweden. During the first year after diagnosis, patients were grouped according to BMI change: 'Increase', or ≥ +1 BMI unit; 'unchanged', or between +1 and–1 BMI unit; and 'decrease', or ≤ –1 BMI unit. Associations between BMI change and CVD mortality, defined as death from stroke, myocardial infarction or sudden death, were estimated using adjusted Cox proportional hazards models (NCT 01121315).

Results. – Baseline mean age was 60.0 years and mean BMI was 30.2 kg/m^2. Patients were followed for up to 9 years (median: 4.6 years). During the first 18 months, 53.4% had no change in their BMI, while 32.2% decreased and 14.4% increased. Compared with patients with unchanged BMI, those with an increased BMI had higher risks of CVD mortality (hazard ratio: 1.63, 95% CI: 1.11–2.39) and all-cause mortality (1.33, 1.01–1.76). BMI decreases had no association with these risks compared with unchanged BMI: 1.06 (0.76–1.48) and 1.06 (0.85–1.33), respectively.

Conclusion. – Increased BMI within the first 18 months of type 2 diabetes diagnosis was associated with an increased long-term risk of CVD mortality. However, BMI decrease did not lower the long-term risk of mortality.

Keywords: Epidemiology; Type 2 diabetes; Weight control; Cardiovascular disease mortality

Résumé

Impact des modifications de l'IMC après le diagnostic de diabète de type 2 sur le risque à long terme de mortalité cardiovasculaire chez 8486 patients en soins primaires.

Objectif. – Un indice élevé de masse corporelle (IMC) est associé à un risque accru de diabète de type 2 et de maladies cardiovasculaires (CV). Nous avons étudié l'association entre l'évolution de l'IMC au cours des 18 mois après le diagnostic du diabète de type 2 et le risque de mortalité CV à long terme.

Méthodes. – Un total de 8486 patients diabétiques de type 2 nouvellement diagnostiqués et sans antécédent de cancer ou de maladies CV issus de 84 centres de soins primaires en Suède ont été étudiés. Au cours de la première année après le diagnostic, les patients ont été regroupés en fonction de l'évolution de l'IMC (augmentation ≥ 1 unité d'IMC; « inchangé » = entre +1 et –1 unité d'IMC ; « diminution » ≤ –1 diminution unité d'IMC). Les associations entre l'IMC et la mortalité CV, définie comme le décès par accident vasculaire cérébral, infarctus du myocarde ou mort subite, ajustées ont été estimées par des modèles de Cox à risques proportionnels.

Résultats. – L'âge moyen à l'inclusion était de 60,0 ans et l'IMC moyen de 30,2 kg/m^2. Les patients ont été suivis pendant neuf ans (médiane de 4,6 ans). Pendant les 18 premiers mois, 53,4 % n'ont pas changé leur IMC, 32,2 % ont eu une diminution, et 14,4 % une augmentation. Par rapport aux patients avec un IMC inchangé, le groupe présentant une augmentation de l'IMC avait un risque plus élevé de mortalité CV (HR: 1,63

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[IC 95 %: 1,11–2,39]) et de mortalité toutes causes (HR: 1,33 [1,01–1,76]). La diminution de l'IMC ne modifiait pas le risque de mortalité (HR: 1,06 [de 0,76– 1,48] et 1,06 [0,85–1,33]) respectivement.

Conclusion. – L'augmentation de l'IMC au cours des 18 premiers mois après le diagnostic de diabète de type 2 est associée à une augmentation à long terme du risque de mortalité cardiovasculaire. La diminution de l'IMC ne modifie pas le risque de mortalité.

Mots clés : Épidémiologie ; Diabète de type 2 ; Le contrôle du poids ; La mortalité cardiovasculaire

1. Introduction

Weight control or the attainment of optimal body weight is a recommended treatment goal in type 2 diabetes patients based on the subsequent beneficial effects on cardiovascular disease (CVD) risk factors [1–3]. The suggested CVD risk reduction with weight loss has been supported by one small observational study of diabetes patients and by extrapolated data from non-diabetic populations [4]. Bariatric surgery for severe obesity with sustained and substantial weight losses of 14–25% over several years has also shown significantly reduced risk of mortality compared with untreated patients [5]. However, the Look AHEAD (Action For Health in Diabetes) trial was prematurely terminated in 2012 because it failed to demonstrate any associations between CVD risk and sustained moderate weight loss in diabetic patients using prospective lifestyle interventions [6]. The clinical effect of weight loss on CVD in the context of routine lifestyle changes in general diabetes care has previously been debated and remains unsettled in the light of recent results [6,7]. Weight gain has been reported to be associated with increased CVD risk in diabetic patients; however, clinical interpretation is difficult due to the secondary nature of the results and the methods used for weight-change calculations [8,9]. Indeed, the importance of weight changes in type 2 diabetes patients on fixed outcomes is currently unclear, thereby supporting the need for new studies addressing this issue.

The objective of the present study was to investigate the association between weight change and risk of CVD mortality in a large primary-care-based sample of patients with newly diagnosed diabetes in a real-world setting.

2. Methods

The study was based on the Retrospective Epidemiological Study to Investigate Outcome and Mortality with Glucose-lowering Drug Treatment in Primary Care (ROSE) study [10]. In 2010, patients' data were extracted from 84 primary-care centres in Sweden, using the Pygargus Customized Extraction Program (CXP) [11], to constitute a representative sample of both publicly and privately owned primary-care centres (61% and 39%, respectively) [12,13]. The 84 centres selected made up approximately 8% of the total number of primary-care centres in Sweden. All data were extracted for the 58,326 patients diagnosed with type 2 diabetes between 1999 and 2009. The diagnosis was identified by the registered diagnostic code and/or prescription of any blood glucose-lowering drug [10]. The International Statistical Classification of Diseases and Related Health Problems (ICD) is used to classify diagnoses in both hospital and primary care in Sweden, and codes 250 (ICD 9) and E10–E14 (ICD 10) were used to identify type 2 diabetes. The Anatomical Therapeutic Chemical (ATC) classification system code A10 was used to identify the prescription of glucose-lowering drugs.

Patients were excluded from the study cohort if they had a previous history of prevalent diabetes from 1987 up to the data-extraction date, or were aged either less than 35 years or more than 79 years, or newly diagnosed with diabetes after 2008. Patients aged less than 35 were excluded to lower the risk of type 1 diabetes patients in the main data extraction from the ROSE study. The exclusion of patients aged more than 79 years was decided upon because they were considered to have little benefit from weight loss and low risk of weight gain. In addition, subjects were excluded if they had a history of CVD, active cancer or missing data on BMI at baseline and within 18 months of the diabetes diagnosis (Supplementary patient flow chart, Fig. S1). Patients were also excluded from analyses if they developed CVD or cancer during the time between the two BMI measurements.

BMI was mainly chosen because it reflects body composition (underweight, normal weight, overweight or obese), which determines the risk of different weight changes [14]. Changes in weight were assessed by calculating BMI changes within the first 18 months of being newly diagnosed with diabetes. Baseline BMI was defined as the closest registration found in the interval from 15 months before to 45 days after the time of newly diagnosed diabetes. The second BMI was sought in the interval from 46 days to 18 months after newly diagnosed diabetes, using only the last registration if several readings were found. BMI change was calculated by subtracting the baseline BMI from the second BMI, after which the patients were divided into three BMI groups: increased, or more than or equal to +1 BMI unit; unchanged, or +1 to–1 BMI unit; and decreased, or less than or equal to –1 BMI unit. The mean interval duration between the index and second BMI in the increased, unchanged and decreased groups was 1.1, 1.0 and 1.0 year, respectively.

2.1. Outcome and covariates

Follow-up time started after the second BMI measurement, and all patients were followed until death or the last date for extracting data from registers. The primary endpoint CVD mortality included all primary causes of death diagnosed with ICD-10 codes I00–I99. Non-fatal CVD comprised myocardial infarction (ICD-9 code 410; ICD-10 code I21), unstable angina (ICD-9 411; ICD-10 I20.0), heart failure (ICD-9 428; ICD-10 I11.0, I50), atrial fibrillation (ICD-9 427; ICD-10 I48), haemorrhagic and embolic stroke (ICD-9 430–438; ICD-10 I60,