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Original article

Anthropometrics indices of obesity, and all-cause and cardiovascular disease-related mortality, in an Asian cohort with type 2 diabetes mellitus

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Abstract

Aim. – The study investigated the relationship of general (body mass index [BMI]) and central (waist circumference [WC]; waist–hip ratio [WHipR]; waist–height ratio [WHeightR]) adiposity with all-cause and cardiovascular disease (CVD)-related mortality in an Asian population with diabetes.

Methods. – A total of 13,278 participants with type 2 diabetes mellitus (T2DM) recruited from public-sector primary-care and specialist outpatients clinics in Singapore were followed-up for a median duration of 2.9 years, during which time there were 524 deaths. Cox proportional-hazards regression and competing-risk models were used to obtain hazard ratios (HRs) for anthropometric variables of all-cause and CVD-related mortality.

Results. – After adjusting for BMI, the highest quintiles of WC, WHipR and WHeightR were all positively associated with mortality compared with the lowest quintiles, with WHeightR exhibiting the largest effect sizes [all-cause mortality HR: 2.13, 95% confidence interval (CI): 1.33–3.42; CVD-related mortality HR: 3.42, 95% CI: 1.62–7.19]. Being overweight but not obese (BMI: $\geq$ 23.0 but < 27.5 kg/m^2) was associated with a decreased risk of CVD-related mortality in those aged $\geq$ 65 years (HR: 0.47, 95% CI: 0.29–0.75), but not in those aged < 65 years (HR: 1.11, 95% CI: 0.49–2.50).

Conclusion. – Overweight, but not obesity, was associated with a reduction in risk of mortality. This was seen in T2DM patients aged $\geq$ 65 years, but not in those younger than this. At the same BMI, having higher central-obesity indices such as WC, WHipR and WHeightR also increased the risk of mortality.

Keywords: Short-term mortality; Diabetes mellitus; Obesity; Central obesity; Anthropometric indices

1. Introduction

Obesity and type 2 diabetes mellitus (T2DM) are major causes of morbidity and mortality in both the developed and developing countries, affecting an estimated 500 million [1] and 382 million [2] adults worldwide, respectively. In particular, the prevalence of obesity [3] and T2DM [4] has increased sharply in Asia over just a few decades.

Among anthropometric indices, body mass index (BMI) with all-cause and cardiovascular disease (CVD)-related mortality has been the most widely studied. A high BMI and increased risk of all-cause and CVD-related mortality have been reported in both Western [5] and Asian [6] healthy populations. However, the same relationship is unclear in people with chronic diseases such as T2DM. BMI has been reported to exhibit inverse [7], positive [8], null [9], and U-shaped [10] associations with all-cause

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mortality in patients with T2DM. In a prospective study with a 10-year follow-up, age was a reported effect-modifier in the relationship between BMI and mortality in an Italian population with T2DM, where a high BMI ($\geq$ 29.9 kg/m^2) was protective in those aged $\geq$ 65 years, but not in those aged < 65 years [7].

The inconsistent findings between obesity and overweight for mortality risk in people with T2DM may possibly be explained by the use of BMI only, as this is a general obesity indicator that does not distinguish fat from lean mass or reflect body fat distribution [11]. The relationship between anthropometric variables of central obesity, such as waist circumference (WC), waist–hip ratio (WHipR) and waist–height ratio (WHeightR), and mortality has also been evaluated [12]. A meta-analysis of nine cohort studies involving 82,864 British participants showed WC and WHipR to be better predictors of CVD-related mortality than BMI in healthy populations [13]. Although fewer studies have been performed in diabetic populations, similar results have been reported. In a cohort study of 6412 European adults with diabetes, the strongest association between anthropometric variables of obesity and all-cause mortality was found with WHeightR in the fifth quintile ($\geq$ 0.64), with a hazard ratio (HR) of 1.88 [95% confidence interval (CI): 1.33–2.65] for men and 2.46 (95% CI: 1.46–4.14) for women [14].

Most of these studies were conducted in Western populations with T2DM. To the best of our knowledge, very few studies have examined the association of such variables of obesity with all-cause and CVD-related mortality in Asian T2DM populations. As Asian populations have different body builds, percentages of body fat and fat distributions, health risks for the same anthropometric index cut-off points may differ from their Western counterparts [15]. For this reason, the present study has investigated the relationship between general adiposity (measured by BMI) and central adiposity (measured by WC, WHipR and WHeightR) and all-cause and CVD-related mortality, and assessed in exploratory analyses whether various sociodemographic factors (age, gender, ethnicity and education level) and smoking status modified these associations in a diabetic Asian population.

2. Methods

2.1. Study population

Data were taken from the Diabetic Cohort (DC) of the Singapore Consortium of Cohort Studies (SCCS) set up to investigate genetic and lifestyle factors and their interaction as risks for common chronic diseases (http://www.nus-cme.org.sg/home.html). Inclusion criteria for the DC included adult Singaporeans and permanent residents followed-up at a public-sector primary care or hospital outpatients' clinic for T2DM. Diagnoses of T2DM had been made by physicians on the basis of clinical signs and symptoms, and biochemical and immunological tests. Those with type 1 diabetes mellitus were not included. All 13,278 participants recruited gave their informed consent, including consent for data linkage with national registries when recruitment was closed in 2010. The National University of Singapore Institutional Review Board approved the study.

2.2. Anthropometric variables

All participants underwent personal interviews and health examinations for anthropometric assessment. Measurements were performed by trained research nurses using standardized protocols [15,16]. Height and weight were measured using stadiometers and weighing scales, respectively [15]. Waist and hip circumferences were measured with a measuring tape placed 1 cm below the umbilicus and at the iliac crest, respectively [16]. Also used were the widely accepted cut-off points for BMI, WC, WHipR and WHeightR established by the World Health Organization (WHO) [15,16]. Quintiles were created for these measures as well as gender-specific quintiles for WC and WHipR, as the internationally accepted cut-offs for these differ between men and women.

2.3. Determination of endpoints

Mortality data were obtained from the National Registry of Diseases Office. Reporting of deaths is mandatory by law, and death registration is complete in Singapore. Our study used the primary cause of death given in the death certificate [using the International Classification of Diseases code version 9 (ICD-9)], while codes 394.0 to 459.0 were considered to be CVD-related mortality. Survival time was computed as the time between date of study recruitment and date of death or censoring on 31 December 2011. Of the 13,278 participants, there were 524 deaths during the follow-up period.

2.4. Statistical analysis

All analyses were performed using SPSS version 20 software (SPSS Inc., Chicago, IL, USA). The statistical significance level was set at $P < 0.05$. Descriptive statistics were used to examine differences in sociodemographic and T2DM-related characteristics according to the BMI cut-off categories for Asians [15]. The Chi^2 test was used for discrete variables, and analysis of variance (ANOVA) for continuous variables. Survival data were modelled on a Cox proportional-hazards regression model, which was used to obtain the HR between anthropometric variables and all-cause mortality, and assumptions were tested through regression analysis of Schoenfeld residuals in relation to time; these were not violated. The time scale used in the Cox model was years.

For cause-specific mortality, deaths from causes other than the primary interest were regarded as competing risks [17]. CVD-related mortality was the primary event of interest and all other causes (such as cancer) were modelled using competing-risks regression [18]. Models were adjusted for age (continuous), gender (males *vs.* females), ethnicity (Malays, Indians and Other *vs.* Chinese), education (primary, secondary, polytechnic/institute of technical education/A levels and university *vs.* no