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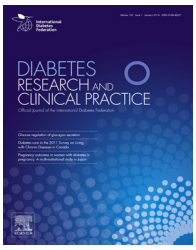

The prognostic role of body mass index on mortality amongst the middle-aged and elderly: A competing risk analysis

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ABSTRACT

Aims: To determine the relationship between body mass index (BMI) including its 5-year changes and mortality, and compare the results obtained using Cox and competing risks models.

Methods: Our study subjects included 2216 persons aged ≥49 years who participated in the Blue Mountains Eye Study, Australia between 1992 and 1994, and returned for further follow-up examinations between 1997 and 1999. We examined the relationship between BMI and mortality using cubic spline. The Cox and competing risks models were used to assess the associations between baseline BMI and its 5-year changes with all-cause and cause-specific mortality.

Results: Amongst subjects aged ≤70 years, the relationship between BMI and all-cause mortality was U-shaped. For those aged >70 years, an L-shaped relationship was seen with no elevation in risk amongst the overweight/obese. Based on the competing risks model, obesity at baseline was associated with increased risk of cardiovascular death and reduction in BMI at 5-year was linked to an increase risk of cancer death amongst those aged ≤70 years. The cause-specific Cox model showed that reduction in BMI at 5-year was associated with cancer-death regardless of age, and with cardiovascular deaths among subjects aged ≤70 years. Cox regression model showed larger magnitude of effect with wider confidence interval as compared with competing risks model.

Conclusions: Conditions associated with obesity are more likely to affect mortality among subjects aged ≤70 years, but not among those aged over 70 years. Cox model shows larger magnitude of effect in comparison with competing risks model.

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1. Introduction

The prevalence of obesity in younger adults and elderly will increase, with significant consequences for public health care [1,2]. Obesity is commonly associated with hypertension, diabetes, cardiovascular disease (CVD) and disability [1,2].

Previous prospective cohort studies have tried to describe the impact of obesity on all-cause and cause-specific mortality, however, conflicting results remains amongst middle-aged and elderly, with a lack of evidence to prove the strength of association between obesity and mortality [3–12]. Variation in age of participants in different studies may contribute to the conflicting findings in these studies, with some studies suggesting that overweight and obesity may not be a risk factor for mortality in the elderly [11,12]. Moreover, the impact of changing BMI over a period of time on mortality remains uncertain [13]. Some studies reported that an increase or decrease in BMI over time predicts a greater risk of CVD, cancer or all-cause mortality among middle-aged or elderly [14–17], while others have not noted this association [4,18].

Additionally, obesity is associated with increases in mortality from multiple causes. Most studies that have examined the associations between obesity and cause-specific mortality fail to take into account ''competing risks'' from other causes of death. Cox regression model is adequate when competing risks are rare (i.e. among younger adults). However, in the presence of strong competing risks, as with frail or elderly populations [19], standard Cox regression model may substantially overestimate the absolute risk of event of interest, because subjects with a competing (and thus censored) event are treated as if they could experience the event of interest in the future [20]. In addition, predictions from a standard survival analysis in the presence of competing risks have been said to refer to the risk of failing from the event of interest in a virtual world where the competing risk is absent [21–23]. For clinical decision-making in the real world, where competing risks do occur, actual rather than virtual absolute risks are often more relevant [24,25]. Therefore, competing risks models are well suited for outcomes involving multiple failure types (such as cancer- and cardiovascular-deaths), as it appropriately account for each competing risk in the analysis, yielding a more accurate estimation of exposure (BMI) effect on different causes of death [20,26]. To our best knowledge, competing risk models have not been used to evaluate the relationship between BMI and its changes with cause-specific mortality.

Therefore, in this study, we sought to determine the associations between baseline BMI, the 5-year change in BMI, with all-cause and cause-specific mortality in the Blue Mountains Eye Study (BMES), and compare the results obtained using standard survival models such as the Kaplan–Meier and Cox with the competing risks model.

2. Materials and methods

2.1. Participants

The BMES is a prospective cohort study of vision and other health outcomes [27] in white Australians. Two adjoining urban postcode areas in the Blue Mountains area, west of Sydney, in New South Wales, Australia, were selected as target population. All non-institutionalised, permanent residents aged 49 years and over at the time of the census were eligible. Permanent residents were defined as living in the dwelling for more than six months of a year [28]. At baseline examination (1992–1994), 3654 (82.4%) of eligible subjects were interviewed and examined. At 5-year follow-up (i.e. between 1997 and 1999), 2335 participants (63.9% of the original cohort or 75.1% of survivors) were examined. Mortality subsequent to the 5-year visits was assessed via demographic data linkage to the Australian National Death Index (NDI) database. Each examination survey of this cohort was approved by the Human Research Ethics Committees of the Western Sydney Area Health Service and the University of Sydney, and the study adhered to the Helsinki Declaration. Signed informed consent was obtained from all participants at each examination. More details of the BMES have been described previously [27,28].

In this study, we included 2216 subjects with complete information from both the baseline and 5-year examinations. Participants who died shortly after the study baseline visits were excluded from the analysis as in a previous study [4], to control for the relation between reduced BMI, morbidity and early death [29].

2.2. Data collection

At each visit, a comprehensive questionnaire comprising demographic information, smoking status (current, former and never smoker), alcohol intake (gram per week) and a detailed history of diseases, including hypertension, diabetes, angina, acute myocardial infarction (AMI), stroke and cancer as well as medication was recorded at face-to-face interviews using a standardised questionnaire conducted by trained interviewers [27]. We defined pre-existing disease(s) as a binary variable based on past history or medication of at least one of the above-mentioned diseases. In addition, self-reported physical activity based on time spent on activities per week using the International Physical Activity Questionnaire [30] were collected. The activities captured included occupational, household and leisure activities.

2.3. Study factors

Participants had their weight (after removal of shoes and heavy clothing) measured by standing on an automated scale, to which a vertical height measure was attached [31]. The BMI was calculated as weight (kg)/height (m^2). Baseline BMI was re-categorised using the classification of the World Health Organisation Expert Committee on Physical Status [32]: underweight: $<18.5\ kg/m^2$, normal weight: 18.5 to $<25\ kg/m^2$, overweight: 25 to $<30\ kg/m^2$, and obese: $\geq 30\ kg/m^2$. Normal weight was considered as the reference group in all analyses.

Five-year change in BMI from baseline was categorised as follows: stable: <1 BMI unit change, gain: ≥ 1 BMI unit gain, reduction: ≥ 1 BMI unit loss [17]. Stable BMI was regarded as the reference group in all analyses involving changes in BMI from the baseline to 5-year visit.