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The Association of Weight loss, Weight status, and Abdominal Obesity with all-cause Mortality in Older Adults

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Short Title: Weight loss, Weight status, and Abdominal Obesity with all-cause Mortality

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Abstract

Objectives: The objectives of this study were to examine whether weight loss, weight status (based on body mass index [BMI] categories), and abdominal obesity (based on waist circumference [WC]) were associated with a 17-year mortality risk in community-dwelling older adults.

Methods: Participants were 2017 community-dwelling adults aged 65 years or above in the longitudinal ESPRIT study. Self-reported weight loss was collected at baseline during face-to-face interviews. Bodyweight (kg), height (m), and waist circumference (cm) were independently measured at the baseline. BMI was categorised as follows: underweight (BMI <18.5kg/m²), normal weight (18.5kg/m² to 24.9kg/m²), overweight (25kg/m² to 29.9kg/m²), and obese (≥30kg/m²). Abdominal obesity was defined by a WC of ≥102cm in men and ≥88cm in women. Adjusted Cox proportional hazards models were used to examine associations of weight loss, weight status, and abdominal obesity with all-cause mortality.

Results: Over 17 years of follow-up (median 15.5 years), 812 participants died. Abdominal obesity compared to non-abdominal obesity was associated with a 49% increased mortality risk (95% CI 1.22-1.83). However, being overweight (but not obese) was associated with a 20% decreased risk (95% CI 0.66-0.97) compared to a normal BMI. Gender did not affect these associations. In the whole cohort, self-reported weight loss at baseline was not associated with an increased mortality risk after adjusting for health and lifestyle factors. However, in men, a baseline self-reported recent weight loss of >3kg was associated with a 52% increase in mortality risk (95% CI 1.05-2.18) in a fully adjusted model.

Discussion/Conclusion: In community-dwelling adults aged ≥65 years, abdominal obesity was strongly associated with increased mortality risk. Being overweight appeared, however, to be protective against mortality. Modest self-reported weight loss was not associated with all-cause mortality in community-dwelling older adults after adjusting for health and lifestyle factors. However, men reporting recent weight loss of more than 3kg may be at increased risk. The findings of this study support the use of waist circumference, rather than BMI, as a predictor of mortality risk in older adults.

Introduction

Obesity has emerged as a major public health issue, with the global prevalence having tripled since 1975 [1]. While obesity affects all age groups, it is increasingly common in older adults [2]. While there is extensive evidence that obesity is associated with an increased risk of cardiovascular disease, cancer, and mortality in younger and middle-aged adults [3], the relationship between obesity and mortality in older adults requires further research [2]. A meta-analysis by Flegal and colleagues found that a body mass index (BMI) in the overweight range (25 kg/m^2 – 30 kg/m^2) was associated with a lower risk of all-cause mortality in older adults compared to those of a healthy weight (BMI between 18.5 kg/m^2 and $<25 \text{ kg/m}^2$), while grade 1 obesity (BMI between 30 kg/m^2 and $\leq 35 \text{ kg/m}^2$) had a similar mortality risk to those in the healthy BMI category [4]. BMI is a crude measure of body composition, and a BMI of $\geq 30 \text{ kg/m}^2$ could encompass a wide range of proportions of lean mass to fat mass. Abdominal obesity, which is defined as abdominal fat accumulation measured by the waist circumference (WC) [5], may be a more appropriate measure of risk, particularly in older adults. Notably, the significant growth of the world's ageing population means that health care systems face significant challenges regarding ageing-related chronic diseases that are either associated with or exacerbated by obesity.

A meta-analysis of 17 studies reported a 67% increase in the risk of mortality with weight loss among older adults (≥ 60 years) [6]. Another recent systematic review and meta-analysis of 35 studies examining the association between weight change and all-cause mortality in older adults, found that weight loss was associated with a 59% increase in the all-cause mortality risk [7]. However, these previous studies did not include consideration of whether baseline weight or abdominal obesity influenced the mortality risks associated with weight loss in community dwelling older adults. As obesity and abdominal obesity could differentially impact the association between weight loss and mortality in later life, this requires further investigation.

As identified in the most recent systematic review [7], only four studies [8-11] investigated the association of weight loss with mortality stratified by the baseline BMI. The findings from this limited number of studies suggested that there may be a stronger association between weight loss and mortality in older adults with an underweight/normal BMI compared to older adults with an overweight/obese BMI. However, the studies used different BMI cut-offs, as follows: one used self-reported weight in early adulthood as the baseline weight [8], and another included only women [10]. It is also unknown whether there are gender-specific differences in the association between weight loss and mortality risk.

The aims of the current study were to examine the association of self-reported weight loss, weight status (based on BMI categories), and abdominal obesity (based on WC) with all-cause mortality

in a large cohort of community-dwelling older adults and to determine whether baseline BMI, WC, or gender affected the association between weight loss and mortality.

Materials and Methods

Study Population

This study utilised data from the population-based, longitudinal Enquête de Santé Psychologique–Risques, Incidence et Traitement (ESPRIT) study [12]. Non-institutionalised French-speaking, older adults aged ≥ 65 years who resided in the Montpellier district in southern France were eligible for enrolment in ESPRIT. The individuals who met the criteria were randomly drawn from 15 electoral rolls across the Montpellier district between March 1999 and February 2001. The ESPRIT study protocol was approved by the Ethical Committee of the University Hospital of Kremlin-Bicetre. Further details of the ESPRIT study have been reported elsewhere [12, 13]. Of the 2,270 participants who were recruited for the ESPRIT study, 241 were excluded from this analysis because they were missing data on recent weight loss, and a further 12 were missing data related to BMI and WC. This left 2,017 participants, who constitute the sample for this study.

Weight Loss, BMI, and WC Measurements

Self-reported weight loss in the last three months was collected as a baseline during face-to-face interviews. Bodyweight (kg), height (m), and waist circumference (cm) [14] were independently measured at baseline in lightly dressed participants. BMI was computed as weight (kg) divided by height (m) squared. Waist circumference was measured between the lower rib margin and the iliac crest following a normal expiration. BMI was categorised according to the World Health Organization's (WHO) definitions as follows: underweight (BMI $< 18.5 \text{ kg/m}^2$), normal weight (18.5 kg/m^2 to 24.9 kg/m^2), overweight (25 kg/m^2 to 29.9 kg/m^2), and obese ($\geq 30 \text{ kg/m}^2$) [15]. Abdominal obesity was defined by a WC of $\geq 102 \text{ cm}$ in men and $\geq 88 \text{ cm}$ in women [15]

All-Cause Mortality

All-cause mortality was ascertained for all participants over a maximum of 17 years of follow-up. Date- and cause- of death was determined from medical records and death registries, as detailed previously [16, 17].

Covariates

Sociodemographic characteristics, lifestyle, and physical health factors was collected at the baseline using a standardised health questionnaire. This included age, gender, smoking status (never smoked, past/current smoker), alcohol consumption ($< 24 \text{ g}$ per day, $\geq 24 \text{ g}$ per day), education level attained (completion of secondary school education), and living situation (alone or with others). Through face-to-face interviews, self-reported information on the history of ischemic pathologies

(angina pectoris, myocardial infarction, stroke, cardiovascular surgery, arthritis, and vascular disease), chronic conditions (high blood pressure, high cholesterol, diabetes, thyroid problems, and asthma), recent cancer, and the diagnosis of current major depressive disorder (MDD), according to DSM-IV criteria,¹² was collected using the Mini-International Neuropsychiatric Interview (MINI, French version 5.00). The depressive symptom severity was assessed using the 20-item inventory by the Centre for Epidemiologic Studies-Depression (CES-D) scale [18], with a cut-off of 16 indicating moderate to severe depressive symptoms.

Statistical Analysis

Summary statistics were reported to describe the frequencies or means (\pm SD) of the baseline characteristics. The chi-square or ANOVA tests were applied to compare the distributions of categorical and continuous variables, respectively, across the weight loss groups. Cox proportional hazard regression models were used to examine the hazard ratio (HR), 95% confidence interval (CI) and P-values for the associations of weight loss, weight status (based on BMI categories), and abdominal obesity (based on WC) with all-mortality. As the mortality risk increases with age, age was used as the time scale, and a baseline age was used as the time origin [19]. The following series of models were constructed: model one was adjusted for gender; model two was additionally adjusted for education, living alone, smoking, alcohol consumption, depression, ischemic pathologies, chronic conditions, and recent cancer; and model three was additionally adjusted for the baseline BMI when analysing self-reported weight loss and abdominal obesity and for baseline WC when analysing the weight statuses. We performed a stratified analysis to examine whether the association between self-reported weight loss and mortality varied by gender or baseline BMI or WC categories.

Sensitivity analyses were undertaken using the final models and repeated with the following changes: (1) participants who died within the first year of the follow-up were excluded to ensure these early deaths did not affect the observed associations; and (2) the five-year follow-up analysis was restricted to test whether shorter follow-up periods influenced the associations.

The statistical data analysis was conducted using STATA version 16 (StataCorp, Texas, USA).

Results

There were 2,017 participants (Table 1) with an average age of 73.3 (SD 5.7) years, and the median follow-up time was 15 years (IQR: 11.2–15.7). During this time, 812 (40.3%) participants died. At the baseline, there were 114 (5.6%) participants who reported a recent weight loss of >3kg, while 219 (10.9%) participants reported having lost between 1kg and 3kg.

Participants who lost between 1kg–3kg had a lower baseline weight compared to the participants who lost >3kg or did not lose any weight. There was a similar pattern for the BMI where the participants

who lost between 1kg–3kg had a lower BMI than the participants who lost >3kg or did not report any weight loss.

The proportion of participants with chronic conditions or cardiovascular ischemic pathologies significantly differed according to the weight loss category, as did depressive symptoms. In all cases, the proportions of individuals with these conditions were highest among individuals with a recent weight loss of >3kg (Table 1).

Association of BMI and WC with All-Cause Mortality

Compared to a 'normal' baseline BMI, being underweight or obese was associated with an increased mortality risk in the minimally-adjusted analysis only (Table 2, Model 1). After adjusting for lifestyle, health factors, and baseline WC, there was no significant association between being underweight or obese and the mortality risk. On the other hand, in the fully adjusted models, being overweight was associated with a 20% lower mortality risk (HR: 0.80, 95% CI: 0.66-0.97, $p=0.02$) compared to a normal weight. The gender did not affect this result ($p=0.71$).

Abdominal obesity was significantly associated with an increased all-cause mortality risk (HR: 1.37, 95% CI: 1.17-1.61, $p<0.001$), even after the multivariate analysis (HR: 1.49, 95% CI: 1.22-1.83, $p<0.001$) in both women and men (Table 2).

Association of Self-reported Weight Loss and Mortality

Compared to no weight loss, a self-reported weight loss of 1kg–3kg was not associated with all-cause mortality in either the minimally-adjusted or fully-adjusted multivariate models (Table 3). In contrast, the participants who self-reported a recent weight loss of >3kg at the baseline compared to those who reported no weight loss had a 44% increased risk of mortality (HR: 1.44, 95% CI: 1.09-1.88, $p=0.008$) when adjusting for age and gender. However, following additional adjustments for other characteristics, including education, living alone, smoking, alcohol consumption, depression, ischemic pathologies chronic conditions, and a recent cancer diagnosis, the association between weight loss and all-cause mortality was no longer significant ($p=0.09$). A further adjustment for the baseline BMI categories did not change this finding ($p=0.07$).

However, the association between weight loss and mortality was affected by gender with some evidence of interaction (Table 3). In the fully-adjusted multivariate models, male participants who lost >3kg had a 52% higher risk of mortality (HR: 1.52, 95%, CI: 1.05-2.18, $p=0.03$) compared to those who

reported no weight loss. No significant association between weight loss and all-cause mortality was observed in women (Table 3).

Effect of Weight Loss and BMI/WC on Mortality Risk

The next step was to determine whether baseline BMI or WC modified the association between baseline recent weight loss and mortality risk. In the Cox regression models, neither interaction term between the baseline BMI and weight loss ($p=0.53$) nor between baseline WC and weight loss ($p=0.39$) was significant. Furthermore, no significant findings were noted in the stratified analyses (Supplementary Table S1). Based on the gender differences in Table 3, gender specific analyses were undertaken, indicating the association between self-reported recent weight loss and mortality risk was only significant for men. Moreover, the baseline BMI and WC did not affect the association between weight loss and mortality in men (Supplementary Table S1).

In the sensitivity analysis, excluding the deaths that occurred within the first year of the follow-up, the result did not vary in both the overall sample and women. However, it was no longer significant in men who lost $>3\text{kg}$ (HR: 1.17, 95% CI: 0.79-1.73, $p=0.42$; Supplementary Table S2). Moreover, by limiting the duration of the follow-up to five years and adjusting for all covariates, we found statistically significant results (self-reported weight loss of 1kg–3kg: HR: 1.76, 95% CI: 1.13-2.73, $p=0.01$; and lost $>3\text{kg}$: (HR: 1.81, 95% CI: 1.03-3.20, $p=0.04$; Supplementary Table S3).

Discussion/Conclusion

In this large population-based study of community-dwelling older adults, for the men, a self-reported weight loss of more than 3kg was associated with a 52% increased mortality risk compared to those who reported no weight loss. However, this was not true for the women, and there was no effect on the baseline BMI or WC categories. Abdominal obesity was associated with a 49% increased mortality risk, while being overweight (but not obese) was associated with a 20% reduced risk compared to a normal weight.

In the present study, we found no overall association between self-reported weight loss and all-cause mortality after considering lifestyle and health factors. This contrasts with the findings of several previous studies and meta-analyses, which reported a significant association between weight loss and all-cause mortality [6, 7]. This could arise from several factors. First, it may be related to the follow-up period, as a previous meta-analysis demonstrated stronger associations between weight loss and mortality in studies with shorter follow-up periods [7]. Indeed, this is supported by the findings of our study. In the sensitivity analysis, when we limited the follow-up period to five years, we observed that a $>3\text{kg}$ weight loss was associated with an 81% increased risk of mortality. In addition, we observed a lower increased risk for individuals who lost between 1kg–3kg. Therefore, weight loss appears to be

a short-term risk factor for mortality. Second, weight loss, particularly if unintentional, can be an indication of impaired health and an underlying disease, which explains the association with an increased risk of mortality. This emphasizes the importance of adjusting for health factors and comorbid conditions, as well as obtaining information on whether the weight loss was intentional or unintentional. Our study, similarly to the vast majority of the previous ones, did not distinguish between intentional and unintentional weight loss [7]. However, there is some evidence that only unintentional weight loss could increase the risk [20]. Our analysis adjusted for a range of comorbid conditions, including cancer [21, 22], unlike several previous studies. It is also possible that adjusting for health condition factors in our multivariate models may have impacted the association, as some of these factors may be biological intermediates in the causal pathway between body weight and mortality rather than confounders [23, 24]. Finally, the age of the participants may also account for differences in the findings between studies.

Our analysis indicated that gender affected the association between self-reported weight loss and all-cause mortality, which was only significant in men. Otsuka et al. [25] examined weight changes in Japanese community-dwelling adults aged 40–79 years and found that the weight of men started to decline when they were aged in their mid-50s, and women’s weight declined when they were in their late-40s [25]. This suggests that there may be gender differences in age-related weight change. However, previous meta-analyses [6, 26] found that of the studies that considered gender differences, the association between weight loss and all-cause mortality was similar in both men and women. We did not find any effect in the initial baseline BMI categories or WC categories; however, we assessed these categories after the weight loss occurred. Due to the lack of previous research on this subject [7], further research is required to fully assess whether BMI or WC categories prior to weight loss influence the relationship between weight loss and mortality.

The associations observed in our study between BMI and all-cause mortality in older adults suggest that being overweight (but not obese) compared to a normal weight was associated with a decreased all-cause mortality risk. This aligns with meta-analyses on the BMI–mortality relationship [4, 27], which reported reduced risks of all-cause mortality in older adults classified as overweight compared to a normal BMI. Additionally, a recent scoping review of observational studies in a community-dwelling population aged 65 years or over reported a reduced risk of mortality for overweight status compared with normal weight status [28]. The WHO BMI classification for body weight (underweight, normal, overweight, obese) is based on data from individuals 18 years and over. The relevance of these classifications for older adults may differ, given the well-known physiological changes observed in body composition with aging, such as loss of muscle and bone mass and fat gain [29]. This may have implications for weight management clinical guidelines, and suggests the need

for careful consideration when using above 'normal' BMI to inform health decision making for community-dwelling adults aged over 65 years.

In our study, abdominal obesity was associated with an increased risk of all-cause mortality. Our finding was consistent with previous studies that examined WC and mortality risk [30]. A meta-analysis of 29 cohort studies by de Hollander et al. [31] reported a greater mortality risk for a higher WC (>88cm women and >102cm men) among adults aged between 65–74 years. With ageing, body fat tends to increase, especially in the abdominal area, which may be linked to an increased metabolic disease risk [32]. This supports mounting evidence that indicates that WC may be a better predictor of all-cause mortality risk compared to BMI in both men and women [33, 34].

The strengths of this study include a large, population-based, prospective study with seventeen-year follow-up of both clinical and environmental factors, which enables extensive covariate adjustment. An additional strength was the validity of the mortality status of the participants, which was obtained using death registries and medical records. In addition, the present study used objectively assessed obesity measures of BMI and WC.

The limitations of this study include self-reporting of weight loss occurring prior to enrolment, which is subject to recall error and an underestimation of the association. Studies have reported that there may be variations between the measured weight and self-reported weight [35, 36]. In addition, the participants were not asked about whether their weight loss was intentional or unintentional, which may have influenced the strength of the association. Unintentional weight loss in later life may reflect an undiagnosed disease or undernutrition, which is linked to mortality. Intentional weight loss may be beneficial for comorbidities, disabilities, and overall health. Physical activity, which has been identified as an important potential confounder in a recent meta-analysis [7], was not available in this study. Furthermore, there were very few underweight participants (3.15% [n=41] women and 0.53% [n=5] men); therefore, the study may be underpowered to examine associations with the underweight status. Finally, a general limitation of cohort studies involving older adults, as in ESPRIT, is selection bias, as study participants reached a minimum of 65 years and needed to be in sufficiently good health to participate in the study. Participants in ESPRIT were also community-dwelling when they were recruited, which precludes generalisation of the findings to frail or institutionalised individuals.

In conclusion, this study of community-dwelling adults aged ≥ 65 years, we found that self-reported weight loss was not associated with all-cause mortality after adjusting for health and lifestyle factors. However, men who reported a weight loss of more than 3kg had an increased mortality risk. Although abdominal obesity was associated with a greater mortality risk in both genders, being overweight, compared to a normal weight, reduced the risk. These findings highlight the importance of healthcare providers to monitor the weight status in older adults to identify early individuals at risk

of weight loss, which would initiate support strategies to maintain a stable weight. The findings of this study also support the use of central obesity to examine the mortality risk rather than a high BMI among older adults.

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Statement of Ethics

This secondary analysis of data was approved by the Monash University Human Research Ethics Committee, reference number: 22290. Written informed consent to participate in ESPRIT was obtained by ESPRIT investigators.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Tagrid Alharbi: Formal analysis, Investigation, Writing – original draft. Joanne Ryan, Roanne Freak-Poli, Danijela Gasevic: Supervision, Writing - review & editing. Jacqueline Scali, Karen Ritchie, Marie-Laure Ancelin: Resources, Funding acquisition, Writing - review & editing. Alice Owen: Conceptualization, Supervision, Writing - review & editing.

Data Availability Statement

Any requests for data can be sent to the corresponding author

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