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Fat Distribution and Mortality: The AGES-Reykjavik Study

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Abstract

Objective—This study examined associations of regional fat depots with all-cause mortality over 11 years of follow-up.

Design and Methods—Data were from 2187 men and 2900 women, aged 66–96 years in AGES-Reykjavik Study. Abdominal visceral fat and subcutaneous fat, and thigh intermuscular fat and subcutaneous fat were measured by CT.

Results—In men, every standard deviation (SD) increment in thigh intermuscular fat was related to a significantly greater mortality risk (HR:1.17, 95%CI:1.08–1.26) after adjustment for age, education, smoking, physical activity, alcohol, BMI, type 2 diabetes and coronary heart disease. In women, visceral fat (per SD increment) significantly increased mortality risk (HR:1.13, 95%CI: 1.03–1.25) while abdominal subcutaneous fat (per SD increment) was associated with a lower mortality risk (HR:0.70; 95%CI:0.61–0.80). Significant interactions with BMI were found in women indicating that visceral fat was a strong predictor of mortality in obese women while abdominal and thigh subcutaneous fat were associated with a lower mortality risk in normal and overweight women.

Conclusions—Fat distribution is associated with mortality over 11 years of follow-up independent of overall fatness. The divergent mortality risks for visceral fat and subcutaneous fat in women suggest complex relationships between overall fatness and mortality.

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Conflict of interest

The author report no conflict of interest

Author contributions: AK conceptualized the study idea, performed the statistical analyses and wrote the paper; RAM contributed to writing the paper and interpreted the data. GE, TA, SS, TFL, VG, LJL interpreted the data and critically reviewed the paper. TBH conceptualized the study idea, interpreted the data and critically reviewed the paper. All authors approved the final version of the paper

Keywords

Body Fat Distribution; Body Composition; Mortality; Obesity; Aged

Introduction

The prevalence of obesity in old age is increasing and is strongly associated with poor health and physical function (1; 2). The association between body weight and mortality is however still somewhat controversial; many studies report an increased mortality risk in the underweight and obese while being overweight has been associated with a both increased and decreased mortality risk. A recent meta-analysis shows that overweight was associated with significantly lower all-cause mortality and a body mass index (BMI) greater or equal to 35 was related to a significantly higher all-cause mortality (3). The association between BMI and mortality is less pronounced in older adults (4; 5). and BMI in old age may not be the best indicator for total fat mass (6)

The distribution of body fat is more important and strongly associated with health outcomes than total adiposity. Particularly, increased visceral or abdominal fat has been related to a greater risk of metabolic diseases (7; 8) independent of overall adiposity (9; 10). Greater intermuscular thigh fat has also been related to poor health outcomes such as poorer glucose tolerance (8). Subcutaneous thigh fat in contrast has been associated with more favorable metabolic risk factors (11).

At present there are very few studies that examined the association between fat distribution and all-cause mortality. A greater waist circumference has been associated with a greater all-cause mortality risk even after adjustment for BMI (12; 13). Waist circumference is often used as a proxy measure for visceral adiposity (14; 15), however, the visceral fat-mortality association need to be confirmed by studies that have direct measures of visceral fat which are limited at present (16–18). Further, it is not clear how fat accumulation in other depots in the abdomen and thigh are associated with mortality.

The present study examined the association between abdominal fat (visceral and subcutaneous fat) and thigh fat (intermuscular and subcutaneous fat) with all-cause mortality independent of overall adiposity in a large study of older adults.

Methods

Study Population

The Reykjavik Study cohort originally comprised a random sample of 30,795 men and women born in 1907–1935 and living in Reykjavik in 1967. A total of 19,381 people attended, resulting in 71% recruitment rate. Between 2002 and 2006, the Age, Gene/Environment Susceptibility (AGES)-Reykjavik (AGES-Reykjavik) Study re-examined 5764 survivors of the original cohort who had participated before in the Reykjavik Study (19). The AGES-Reykjavik Study was approved by the institutional review boards of the National Institute on Aging, the National Bioethics Committee (VSN: 00-063) and the Data Protection Authority. The comprehensive baseline examination using imaging techniques

included a detailed medical history, physical examination, physical performance tests, body composition examination, cognitive tests, laboratory and screening tests, and questionnaires on health-related behaviors. Written informed consent was obtained from all study participants. A total of 5087 participants were included in the present analyses, 488 participants were excluded because of missing body composition data: 79 participants were excluded that were underweight defined as BMI<18.5 kg/m^2; and 110 participants had missing data on covariates.

Measures

Body composition—Computed tomography imaging of the mid-thigh and abdomen at the L4/L5 vertebrae was performed with a 4-row detector system (Sensation; Siemens Medical Systems, Erlangen, Germany). Visceral adipose tissue and abdominal subcutaneous adipose tissue were estimated from a single 10mm thick trans-axial section. Images were loaded into an AVS5 display environment. Visceral adipose tissue was distinguished from subcutaneous adipose tissue by tracing along the facial plane defining the internal abdominal wall. Adipose areas were calculated by multiplying the number of pixels by the pixel area using specialized software (University of California, San Francisco). Thigh subcutaneous fat and intermuscular fat were estimated from a single 10mm thick axial image from the femoral midpoint by manually drawing a line along the deep fascial plane surrounding the thigh muscles. The thigh fat depots for the right and left thigh were added.

Mortality—All-cause mortality was ascertained from the Icelandic National Roster (http://www.statice.is/Statistics/Population/Births-and-death) through September 2013.

Covariates—Covariates included age, level of education, smoking status, physical activity, alcohol consumption, BMI, type 2 diabetes, and coronary heart disease. Level of education was classified into four categories: primary school, secondary, college, and university. Smoking was categorized as never, former, or current cigarette smoker. Physical activity was assessed by one question on the frequency of moderate to vigorous physical activity 1 year prior to baseline. Alcohol consumption was assessed by a questionnaire about the number of alcoholic drinks per month which was converted into grams of alcohol per week. BMI was calculated from measured height and weight. BMI was also categorized as normal weight (18.5–<25 kg/m^2); overweight (25–<30 kg/m^2); and obese (≥30 kg/m^2). Type 2 diabetes and coronary heart disease were determined from self-report, medication use, and clinical assessment.

Statistical analysis

All analyses were stratified for men and women because of known differences in body composition between men and women. Baseline characteristics were compared between men and women using chi-square tests for categorical variables and t-test for continuous variables. Cox proportional hazard models were used to examine the association between each fat depot and time to death or date of follow-up for censored participants. The Cox proportional hazard assumption was tested and not violated. Hazard ratios (HR) are presented per 1 standard deviation (SD) increment of each adiposity measure. Model 1 was adjusted for age, level of education, smoking status, physical activity, alcohol consumption

which were all considered confounders. Model 2 included all variables of the first model and BMI to understand whether the potential association between the different adiposity measure and mortality are independent of overall body fatness. Model 3 included all variables of model 2 and type 2 diabetes and coronary heart disease. Interactions between each fat depot and covariates were tested. All analyses were conducted with IBM SPSS Statistics 21.

Results

Baseline characteristics of the study population are shown in table 1. The average age of the study population was 76 years old and most people completed a secondary education. Men had significantly more visceral fat, while women had more abdominal subcutaneous fat. Women also had more thigh intermuscular and subcutaneous fat than men. Participants that were excluded from analyses due to missing data or who were underweight were more likely to be women, were significantly older at baseline, and had lower BMI (all $p<0.01$).

During 11 years of follow-up with an average follow-up time of 8 years, 919 men and 882 women died. In women, every SD increment in visceral fat was associated with a significantly increased all-cause mortality risk (HR: 1.16, 95% confidence interval (CI) 1.05–1.28) adjusted for age, education, smoking status, physical activity, alcohol consumption, and BMI (Table 2, model 2). This association remained significant in model 3 after additional adjustment for prevalent diabetes and coronary heart disease. Every SD increment in abdominal subcutaneous fat was associated with a significantly lower mortality risk (HR: 0.70, 95CI: 0.61–0.80) in women (model 3). In men abdominal fat was not associated with mortality.

In men there was a significant association between intermuscular fat and mortality (HR: 1.17, 95%CI: 1.08–1.26, Table 2, model 3) but not in women (HR: 1.01, 95%CI: 0.94–1.09, model 3). Thigh subcutaneous fat was associated with a significantly lower mortality risk in women in model 2 (HR: 0.89, 95%CI: 0.80–0.99) which became non-significant after additional adjustment for prevalent diabetes and coronary heart disease. In additional analyses we adjusted for blood lipid levels (HDL and LDL cholesterol levels and triglycerides) which did not change our results.

Interactions between each fat depot and covariates were tested in both men and women. Significant interactions with BMI were found in women for visceral and abdominal subcutaneous fat and thigh subcutaneous fat (all $p<0.05$). Figure 1 shows the stratified results for women adjusted for all confounders. Visceral fat was significantly associated with mortality in obese women only (HR: 1.47, 95%CI: 1.27–1.70) while abdominal subcutaneous fat was associated with lower mortality in normal weight (HR: 0.60, 95%CI: 0.49–0.74) and overweight (HR: 0.71. 95%CI: 0.58–0.86) women. Thigh subcutaneous fat was associated with a lower mortality risk in normal weight women only and was statistically significant in the normal weight (HR: 0.72, 95%CI: 0.58–0.90).

In additional analyses with both visceral and abdominal subcutaneous fat in a single model in women, visceral remained to be associated with a significantly increased mortality risk

(HR: 1.13, 95%CI: 1.05–.122) and subcutaneous fat with a significantly decreased mortality risk (HR: 0.77, 95%CI: 0.70–0.84).

Additionally we examined the association between BMI and mortality. Compared to normal BMI (18.5–24.9), being overweight (BMI 25.0–29.9) or obese (BMI ≥30) was not associated with mortality in men. Overweight women had a significantly lower mortality risk (HR: 0.80, 95%CI: 0.68–0.93) compared to women with a normal BMI; but obesity was not associated with mortality.

Discussion

This is one of the first large studies examining the association between regional fat depots and all-cause mortality taking into account both fat depots in the abdomen and thigh. Thigh intermuscular fat was associated with a significant increased risk of all-cause mortality in men independent of overall fatness. In women, visceral fat increased the risk of mortality while abdominal subcutaneous and thigh subcutaneous fat was negatively association with mortality; these associations were also independent of overall fatness. Significant interactions with BMI were found in women indicating that visceral fat was a strong predictor of mortality in obese women while abdominal and thigh subcutaneous fat were associated with a lower mortality risk in normal and overweight women. Results also suggest sex differences in regards to adipose distribution and mortality.

Only a few previous studies have investigated the association between fat distribution from radiographic measures of fat and mortality. A large waist circumference has been associated with an increased mortality risk (12; 13), while a large hip-circumference has been associated with a lower mortality risk (20). Although these studies suggest that fat distribution is important they do not distinguish between the specific fat depots in the abdomen and thigh. A small study in 291 men showed that greater visceral fat was related to premature mortality independently from total fat (16). Another recent study also reported a significant positive association between visceral fat and mortality among 733 Japanese Americans (18). In both studies mentioned above, abdominal subcutaneous fat was not significantly associated with mortality. In 3086 men and women from the Framingham Heart Study neither visceral nor abdominal subcutaneous fat were associated with all-cause mortality (17).

Numerous studies have shown that visceral adipose tissue is a metabolic risk factor (7; 8; 21). In our study, an increase in visceral fat is strongly associated with an increased mortality risk in obese women. On the contrary subcutaneous fat was negatively associated with mortality in normal and overweight women. Our finding that subcutaneous fat may actually be protective for mortality in overweight women may explain the observation of many previous studies that did not observe an increased mortality risk in the overweight using BMI as a measure of total adiposity (3). The mortality risk associated with specific adipose depots in our study varied by BMI in women. This shows the complexity of relationships between adipose distribution, BMI and health outcomes and indicates that it is more informative to examine multiple measures of adiposity in relation to health risks.

Adipose tissue is an active endocrine organ that secretes several adipokines (22). Subcutaneous adipose tissue secretes more favorable adipokines, including leptin and adiponectin while visceral adipose tissue is related to more pro-inflammatory markers such as IL-6 and TNF-α (23–26). This may explain the different metabolic effects of these fat depots and the associated mortality risks in the present study. Intermuscular fat has also been related to metabolic risk, inflammation and decreased physical function (8; 23; 27). A recent study in cancer patients shows that increased muscle fat infiltration is associated with lower survival (28). In our study, intermuscular fat associated with an increased risk mortality risk in men independent of overall fatness. Future studies are needed to corroborate our findings.

Strengths include the large sample size and long follow-up period and the precise body composition measures from CT imaging. Some limitations of the study also need to be considered. First, we adjusted for BMI as a measure of total fat mass; however, BMI does not distinguish fat from lean mass. In a smaller sample within our study population, fat mass, assessed by bioelectric impedance was available and adjusting for total percent fat instead of BMI did not change the results. Second, our study consisted of older Caucasian adults so results may not be generalizable to younger age groups and other ethnicities; future studies are needed to examine the effects of regional fat depots in younger ages with mortality.

In conclusion, intermuscular fat was associated with an increased risk of mortality in men. Visceral fat was associated with an increased mortality risk in obese women. Subcutaneous fat was negatively associated with mortality in normal and overweight women. Results indicate that fat distribution is associated with an increased mortality risk independent of overall fatness.

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REFERENCES

1. Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. Am J Clin Nutr. 2005; 82:923–934. [PubMed: 16280421]
2. Wang YC, Colditz GA, Kuntz KM. Forecasting the obesity epidemic in the aging U.S. population. Obesity (Silver Spring). 2007; 15:2855–2865. [PubMed: 18070778]
3. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. JAMA. 2013; 309:71–82. [PubMed: 23280227]
4. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. JAMA. 2005; 293:1861–1867. [PubMed: 15840860]
5. Toss F, Wiklund P, Nordstrom P, Nordstrom A. Body composition and mortality risk in later life. Age Ageing. 2012; 41:677–681. [PubMed: 22820447]
6. Zamboni M, Mazzali G, Zoico E, Harris TB, Meigs JB, Di Francesco V, et al. Health consequences of obesity in the elderly: a review of four unresolved questions. Int J Obes (Lond). 2005; 29:1011–1029. [PubMed: 15925957]

7. Boyko EJ, Fujimoto WY, Leonetti DL, Newell-Morris L. Visceral adiposity and risk of type 2 diabetes: a prospective study among Japanese Americans. Diabetes Care. 2000; 23:465–471. [PubMed: 10857936]
8. Goodpaster BH, Krishnaswami S, Resnick H, Kelley DE, Haggerty C, Harris TB, et al. Association between regional adipose tissue distribution and both type 2 diabetes and impaired glucose tolerance in elderly men and women. Diabetes Care. 2003; 26:372–379. [PubMed: 12547865]
9. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. Am J Clin Nutr. 2004; 79:379–384. [PubMed: 14985210]
10. Zhu S, Wang Z, Heshka S, Heo M, Faith MS, Heymsfield SB. Waist circumference and obesity-associated risk factors among whites in the third National Health and Nutrition Examination Survey: clinical action thresholds. Am J Clin Nutr. 2002; 76:743–749. [PubMed: 12324286]
11. Snijder MB, Dekker JM, Visser M, Bouter LM, Stehouwer CD, Yudkin JS, et al. Trunk fat and leg fat have independent and opposite associations with fasting and postload glucose levels: the Hoorn study. Diabetes Care. 2004; 27:372–377. [PubMed: 14747216]
12. Koster A, Leitzmann MF, Schatzkin A, Mouw T, Adams KF, van Eijk JT, et al. Waist circumference and mortality. Am J Epidemiol. 2008; 167:1465–1475. [PubMed: 18417494]
13. Jacobs EJ, Newton CC, Wang Y, Patel AV, McCullough ML, Campbell PT, et al. Waist circumference and all-cause mortality in a large US cohort. Arch Intern Med. 2010; 170:1293–1301. [PubMed: 20696950]
14. Janssen I, Heymsfield SB, Allison DB, Kotler DP, Ross R. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. Am J Clin Nutr. 2002; 75:683–688. [PubMed: 11916754]
15. Snijder MB, van Dam RM, Visser M, Seidell JC. What aspects of body fat are particularly hazardous and how do we measure them? Int J Epidemiol. 2006; 35:83–92. [PubMed: 16339600]
16. Kuk JL, Katzmarzyk PT, Nichaman MZ, Church TS, Blair SN, Ross R. Visceral fat is an independent predictor of all-cause mortality in men. Obesity (Silver Spring). 2006; 14:336–341. [PubMed: 16571861]
17. Britton KA, Massaro JM, Murabito JM, Kreger BE, Hoffmann U, Fox CS. Body fat distribution, incident cardiovascular disease, cancer, and all-cause mortality. J Am Coll Cardiol. 2013; 62:921–925. [PubMed: 23850922]
18. McNeely MJ, Shofer JB, Leonetti DL, Fujimoto WY, Boyko EJ. Associations among visceral fat, all-cause mortality, and obesity-related mortality in Japanese Americans. Diabetes Care. 2012; 35:296–298. [PubMed: 22190675]
19. Harris TB, Launer LJ, Eiriksdottir G, Kjartansson O, Jonsson PV, Sigurdsson G, et al. Age, Gene/Environment Susceptibility-Reykjavik Study: multidisciplinary applied phenomics. Am J Epidemiol. 2007; 165:1076–1087. [PubMed: 17351290]
20. Lanfer A, Mehlig K, Heitmann BL, Lissner L. Does change in hip circumference predict cardiovascular disease and overall mortality in Danish and Swedish women? Obesity (Silver Spring). 2014; 22:957–963. [PubMed: 23963732]
21. Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich-Horvat P, Liu CY, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation. 2007; 116:39–48. [PubMed: 17576866]
22. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004; 89:2548–2556. [PubMed: 15181022]
23. Beasley LE, Koster A, Newman AB, Javaid MK, Ferrucci L, Kritchevsky SB, et al. Inflammation and race and gender differences in computerized tomography-measured adipose depots. Obesity (Silver Spring). 2009; 17:1062–1069. [PubMed: 19165157]
24. Pou KM, Massaro JM, Hoffmann U, Vasan RS, Maurovich-Horvat P, Larson MG, et al. Visceral and subcutaneous adipose tissue volumes are crosssectionally related to markers of inflammation and oxidative stress: the Framingham Heart Study. Circulation. 2007; 116:1234–1241. [PubMed: 17709633]
25. Lihn AS, Bruun JM, He G, Pedersen SB, Jensen PF, Richelsen B. Lower expression of adiponectin mRNA in visceral adipose tissue in lean and obese subjects. Mol Cell Endocrinol. 2004; 219:9–15. [PubMed: 15149722]

26. Van Harmelen V, Reynisdottir S, Eriksson P, Thorne A, Hoffstedt J, Lonnqvist F, et al. Leptin secretion from subcutaneous and visceral adipose tissue in women. Diabetes. 1998; 47:913–917. [PubMed: 9604868]

27. Beavers KM, Beavers DP, Houston DK, Harris TB, Hue TF, Koster A, et al. Associations between body composition and gait-speed decline: results from the Health, Aging, and Body Composition study. Am J Clin Nutr. 2013; 97:552–560. [PubMed: 23364001]

28. Martin L, Birdsell L, Macdonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. J Clin Oncol. 2013; 31:1539–1547. [PubMed: 23530101]

What is already known about this subject

- The association between BMI and mortality is less pronounced in older adults which is thought to be related to age-related changes in fat distribution
- At present there are very few studies that examined the association between fat distribution, taking into account both fat depots in the abdomen and thigh, and all-cause mortality.

What this study adds

- Intermuscular fat was associated with an increased risk of mortality in men.
- Visceral fat was associated with an increased mortality risk in obese women; subcutaneous fat was negatively associated with mortality in normal and overweight women.
- Fat distribution is associated with mortality independent of overall fatness.

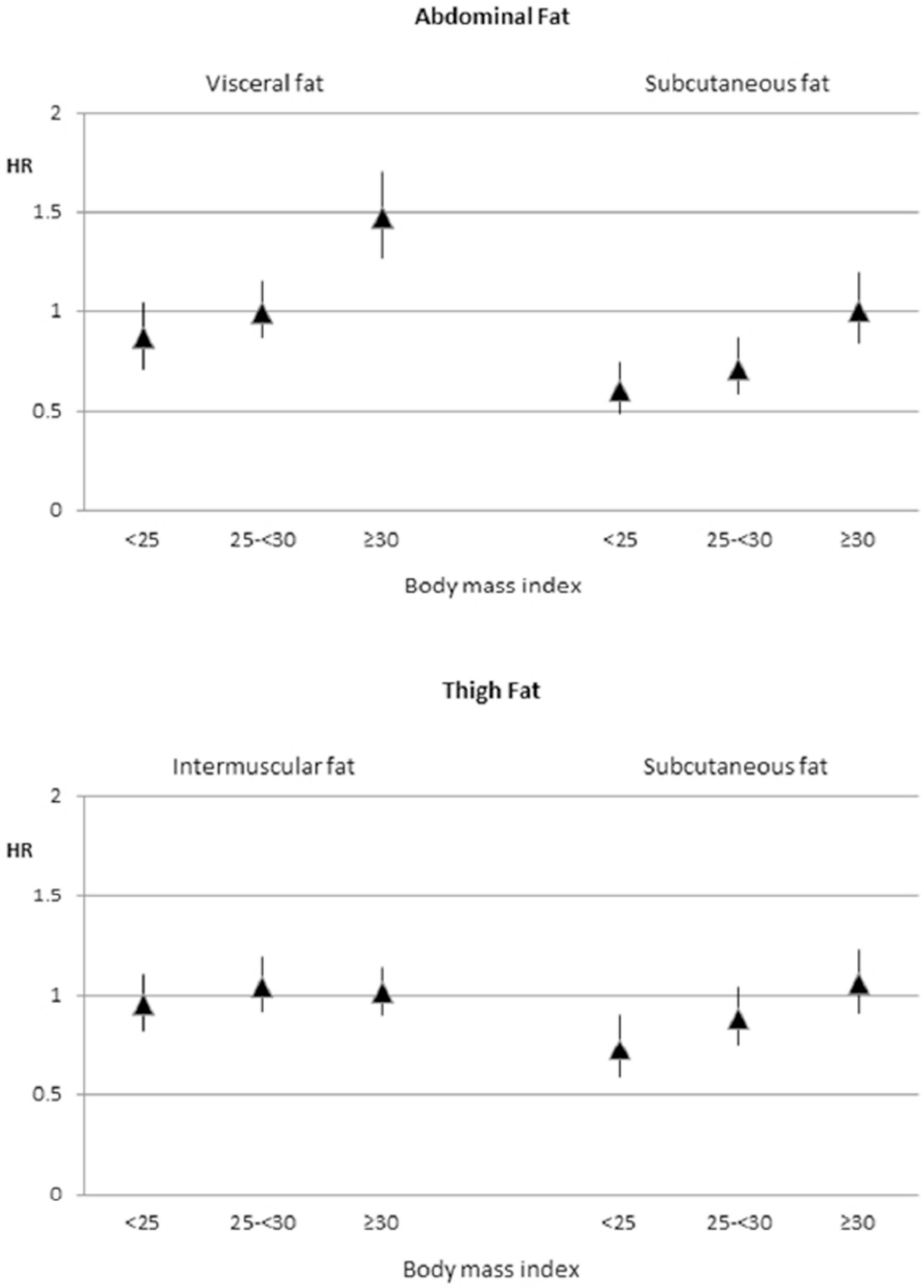

Figure 1.

Hazard ratios[1] ± 95% confidence intervals of mortality in women with measures of abdominal and thigh fat (per SD increment) stratified by BMI group.

[1] Adjusted for age, education, smoking status, physical activity, alcohol consumption, type 2 diabetes, and CHD.

Table 1

Baseline characteristics of the study population

Characteristics	Men N=2187	Women N=2900	p-value
Age (year), mean (SD)	76.6 (5.4)	76.3 (5.6)	0.16
Education, %			
Primary	16.1	29.2	<0.01
Secondary	53.1	47.6	
College	12.5	17.4	
University	18.3	5.9	
Smoking, %			
Never	39.5	53.4	<0.01
Former	54.9	34.7	
Current	5.7	11.9	
Moderate to vigorous physical activity (hours per week), mean (SD)	1.4 (2.4)	1.0 (2.0)	<0.01
Alcohol consumption (g/week), mean (SD)	22.2 (42.6)	9.4 (21.4)	<0.01
Type 2 diabetes, %	15.3	9.5	<0.01
Coronary heart disease, %	31.2	13.6	<0.01
Body mass index (kg/m^2), mean (SD)	26.9 (3.7)	27.3 (4.6)	<0.01
Body mass index group, %			
Normal	31.8	33.0	<0.01
Overweight	49.3	41.9	
Obese	18.9	25.1	
Abdomen			
Visceral fat (cm^2), mean (SD)	204.2 (85.1)	152.1 (65.8)	<0.01
Subcutaneous fat (cm^2), mean (SD)	204.6 (85.7)	298.7 (108.3)	<0.01
Thigh			
Intermuscular fat area (cm^2), mean (SD)	35.8 (16.1)	37.6 (15.8)	<0.01
Subcutaneous fat area (cm^2), mean (SD)	78.4 (38.5)	188.6 (80.9)	<0.01

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Table 2

Hazard ratios and 95% confidence intervals of mortality according to abdominal visceral and subcutaneous fat and thigh intermuscular and subcutaneous fat[1]

	Men						Women					
	Model 1[2]		Model 2[3]		Model 3[4]		Model 1[2]		Model 2[3]		Model 3[4]	
	HR	95%CI	HR	95%CI	HR	95%CI	HR	95%CI	HR	95%CI	HR	95%CI
Abdomen												
Visceral fat	1.00	0.94–1.07	0.97	0.88–1.06	0.96	0.87–1.05	1.03	0.96–1.10	1.16	1.05–1.28	1.13	1.03–1.25
Subcutaneous fat	1.04	0.97–1.11	1.04	0.92–1.17	1.03	0.92–1.16	0.82	0.76–0.89	0.68	0.59–0.77	0.70	0.61–0.80
Thigh												
Intermuscular fat	1.12	1.05–1.20	1.15	1.07–1.24	1.17	1.08–1.26	0.98	0.91–1.05	1.01	0.94–1.09	1.01	0.94–1.09
Subcutaneous fat	1.05	0.99–1.12	1.05	0.97–1.15	1.08	0.99–1.18	0.89	0.83–0.96	0.89	0.80–0.99	0.91	0.82–1.01

[1] HR per SD increment in each fat depot

[2] Model 1 Adjusted for age, education, smoking status, physical activity, and alcohol consumption

[3] Model 2 Adjusted for age, education, smoking status, physical activity, alcohol consumption, and BMI

[4] Model 3 Adjusted for age, education, smoking status, physical activity, alcohol consumption, BMI, type 2 diabetes, and coronary heart disease