Underweight as a Predictor of Diabetes in Older Adults

A large cohort study

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A total of 39,201 men and 88,012 women aged 40–79 years who underwent health checkups in 1993 and who were free of diabetes were followed until the end of 2004 to examine an association between underweight and risk of diabetes. Incident diabetes was defined by a fasting blood glucose concentration ≥7.0 mmol/l or nonfasting glucose ≥11.1 mmol/l and/or diabetes treatment. The multivariable hazard ratio of diabetes adjusted for age, baseline blood glucose level, fasting status, and other confounding variables among subjects who had a BMI <18.5 kg/m^2 compared with those with a BMI 18.5–24.9 kg/m^2 was 1.32 (95% CI 1.12–1.56) in men aged 60–79 years and 1.31 (1.07–1.60) in women aged 60–79 years. Underweight may be associated with risk of diabetes among older adults.

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RESEARCH DESIGN AND METHODS — In the present study, we enrolled 181,863 nondiabetic Japanese subjects (58,402 men and 123,461 women) from community residents aged 40–79 years who underwent health checkups in 1993 conducted by the local governments under the Japan Health Laws. We excluded 19,201 men and 35,449 women who did not participate in the 1994 survey, thereby ensuring that the subjects were followed up for at least 1 year. A total of 39,201 men and 88,012 women were followed up annually until the diagnosis of diabetes mellitus or the end of 2004. Individuals who did not undergo checkups during the follow-up periods were censored on the date of their latest checkup.

At baseline in 1993, height and weight were measured. BMI was calculated as weight in kilograms divided by the square of height in meters. Plasma glucose, serum total cholesterol, triglyceride, and HDL cholesterol were measured. An interview was conducted to ascertain smoking status (never smoked; exsmoker; current smoker, <20 cigarettes per day; and current smoker, ≥20 cigarettes perday) and alcohol intake (never, sometimes, <66 g/day, and ≥66 g/day).

We diagnosed incidence of diabetes when there was a fasting plasma glucose level ≥7.0 mmol/l or a nonfasting plasma glucose level ≥11.1 mmol/l and/or when a person had begun to receive treatment for diabetes. Fasting was defined as not having had a meal for at least 8 h.

HRs for diabetes according to BMI (<18.5, 18.5–24.9, and ≥30.0 kg/m^2) were calculated using a multivariable Cox proportional hazards regression model. Covariates included age (years), baseline blood glucose level (millimoles per liter), fasting status (yes or no), antihypertensive medication use (yes or no), antihyperlipidemic medication use (yes or no), serum total cholesterol level (millimoles per liter), serum HDL cholesterol level (millimoles per liter), log-transformed triglyceride level (millimoles per liter), systolic blood pressure level, smoking status (never smoked; exsmoker; current smoker, <20 cigarettes per day; and current smoker, ≥20 cigarettes per day), and alcohol intake (never, sometimes, <66 g/day, and ≥66 g/day).

RESULTS — Of the 127,213 subjects (39,201 men and 88,012 women), 8,447 developed diabetes (3,863 men and 4,584 women) during a mean of 5.3 years of follow-up (4.9 years for men and 5.4 years for women).

Table 1 shows age-specific HRs of diabetes according to BMI. Compared with subjects with BMI 18.5–24.9 kg/m^2, the multivariable HR for diabetes among subjects with BMI <18.5 kg/m^2 (underweight) was 1.32 (95% CI 1.12–1.56) in men aged 60–79 years and 1.31 (1.07–1.60) in women aged 60–79 years. No significant association was found between underweight and risk of diabetes in either sex aged 40–59 years.

The interaction between age-group and underweight versus BMI 18.5–24.9 kg/m^2 was statistically significant for women (P = 0.012) but not men (P = 0.800).

CONCLUSIONS — To our knowledge, this is the first prospective large-cohort study to show significant associations of low and high BMI with risks of diabetes among older adults. Mechanisms behind the association between low BMI (underweight) and diabetes among older adults are uncertain. Insulin secretion declines in older adults (1); and lean diabetic older adults exhibit a profound impairment in glucose-induced insulin release while obese diabetic older adults do not (2). Several experimental studies using rats showed that protein-calorie malnutrition and magnesium deficiency cause low insulin secretion and a low pancreatic insulin store (3,4). In humans, a study of 556 older adult subjects reported that a poor nutritional status was associated with the prevalence of type 2 diabetes; mean se-

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Table 1—*Age-specific HRs (95% CIs) for incidence of diabetes according to BMI among 39,201 men and 88,012 women in Ibaraki-ken, Japan, 1993–2004*

BMI (kg/m^2)	*n*	Person-years	Incidence rates/1,000 person-years	Age-adjusted HR (95% CI)	Multivariable HR* (95% CI)
Men					
Aged 40–59 years					
<18.5	284	1,176	17.9	1.21 (0.78–1.87)	1.33 (0.85–2.05)
18.5–24.9	8,977	46,547	14.2	1.00 (ref.)	1.00 (ref.)
25.0–29.9	4,180	20,701	22.2	1.53 (1.36–1.73)	1.33 (1.17–1.51)
≥30.0	278	1,230	33.3	2.25 (1.64–3.09)	1.69 (1.22–2.34)
Aged 60–79 years					
<18.5	1,375	5,906	26.4	1.27 (1.08–1.50)	1.32 (1.12–1.56)
18.5–24.9	18,031	87,462	20.2	1.00 (ref.)	1.00 (ref.)
25.0–29.9	5,781	27,348	26.2	1.29 (1.18–1.40)	1.18 (1.08–1.30)
≥30.0	295	1,353	31.8	1.56 (1.16–2.12)	1.33 (0.98–1.81)
Women					
Aged 40–59 years					
<18.5	1,506	8,538	4.6	0.79 (0.57–1.09)	0.87 (0.63–1.20)
18.5–24.9	31,655	185,911	5.9	1.00 (ref.)	1.00 (ref.)
25.0–29.9	10,970	61,582	11.3	1.81 (1.64–1.99)	1.40 (1.27–1.55)
≥30.0	1,236	5,838	31.5	4.93 (4.22–5.77)	2.81 (2.38–3.31)
Aged 60–79 years					
<18.5	1,915	8,953	11.8	1.16 (0.95–1.41)	1.31 (1.07–1.60)
18.5–24.9	26,464	137,095	9.8	1.00 (ref.)	1.00 (ref.)
25.0–29.9	12,904	64,294	15.1	1.54 (1.41–1.67)	1.31 (1.20–1.43)
≥30.0	1,362	5,722	26.2	2.57 (2.17–3.04)	1.85 (1.56–2.20)

*Adjusted for age (years), baseline blood glucose level, fasting status (yes or no), antihypertensive medication use (yes or no), antihyperlipidemic medication use (yes or no), serum total cholesterol level, serum HDL cholesterol level, log-transformed triglyceride level, systolic blood pressure level, smoking status (never smoked; ex-smoker; current smoker, <20 cigarettes per day; and current smoker, ≥20 cigarettes perday), and alcohol intake (never, sometimes, <66 g/day, and ≥66 g/day).

rum albumin levels were lower among diabetic than nondiabetic subjects (5). Furthermore, low dietary magnesium was associated with risk of type 2 diabetes (6).

The strength of the present study comes from the use of a large cohort in which the incidence of diabetes was ascertained by blood glucose levels, as opposed to many previous large-cohort studies by self-administered questionnaire (7,8). On the other hand, our study had several limitations. First, potential confounding factors brought about by physical activity remained because we did not assess this variable. However, physical activity was reported to not substantially alter the association between BMI and risk of diabetes (9). Second, oral glucose tolerance tests were not conducted for diagnosis of diabetes. Third, the follow-up rate was moderate. However, the BMI distributions were similar between the subjects followed and those not followed. Therefore, the results were unlikely to be affected by the participants not followed. Fourth, although we addressed the association between underweight and excess risk of diabetes among older adults, the magnitude of the relationship for whole population might be small because large sample size yields excess statistical power. Finally, the subjects in the present study were residents of only a single prefecture in Japan. In summary, underweight may be associated with risk of diabetes among older adults.

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