BMI and Diabetes Risk in Singaporean Chinese

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OBJECTIVE — Increased BMI is a robust risk factor for type 2 diabetes. Paradoxically, South Asians have relatively low BMIs despite their high prevalence of type 2 diabetes. We examined the association between BMI and incident type 2 diabetes because detailed prospective cohort data on this topic in Asians are scarce.

RESEARCH DESIGN AND METHODS — This study was a prospective analysis of 37,091 men and women aged 45–74 years in the Singapore Chinese Health Study, using Cox regression analysis.

RESULTS — Risk of incident type 2 diabetes significantly increased beginning with BMIs 18.5–23.0 kg/m^2 (relative risk 2.47 [95% CI 1.75–3.48]) and continued in a monotonic fashion across the spectrum of BMI. Results were stronger for younger than for older adults.

CONCLUSIONS — BMIs considered lean and normal in Singaporean Chinese are strongly associated with increased risk of incident type 2 diabetes. This association weakened with advanced age but remained significant.

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Asia is experiencing an epidemic of obesity and type 2 diabetes (1). It is recognized that BMI generally presents a dose-response relation with incidence of type 2 diabetes across populations; however, a clearer understanding of the association between BMI and incident diabetes is needed in lean Asians. Indeed, the World Health Organization has called for more longitudinal research on this topic in Asian populations (2).

RESEARCH DESIGN AND METHODS

— The Singapore Chinese Health Study is a population-based prospective cohort study of ethnic Chinese men and women (Hokkien or Cantonese dialect), aged 45–74 years, living in government-housing estates (which house 86% of all Singaporeans) (3). A total of 63,257 individuals completed in-person interviews between April 1993 and December 1998 using a structured questionnaire that requested information on demographic characteristics, height and weight, tobacco use, physical activity, medical history, and family history of cancer and a validated semiquantitative food frequency section listing 165 food items commonly consumed in the population (3). Follow-up telephone interviews updating health status took place between 1999 and 2004 for 52,325 cohort members (83% of recruited cohort). Diabetes was self-reported. Further details on report and validation of type 2 diabetes status may be found in Odegaard et al. (4).

BMI (weight in kilograms divided by the square of height in meters) was calculated using self-reported height and weight. Person-years for each participant were calculated from the year of recruitment to the year of reported type 2 diabetes diagnosis or the year of follow-up telephone interview for those who did not report a diabetes diagnosis. Cox proportional hazards regression methods were used to examine the associations between BMI and incident type 2 diabetes using SAS statistical software version 9.1 (SAS Institute, Cary, NC). We estimated the hazard ratio (HR) for levels of the exposure variables and the corresponding 95% CI. Participants who died before the follow-up interview (7,722); reported baseline diabetes (5,696), cancer, heart disease, or stroke (5,975); had a missing component of BMI data (6,753); or who were lost to follow-up (<1%) were excluded. A total of 37,091 participants and 1,904 incident cases had full data. Proportional hazards assumptions were not violated. BMI was included as World Health Organization cut points for Asians in Singapore (<18.5, 18.5–22.9, 23–27.49, and >27.5 kg/m^2) and as deciles. Hypothesized tests for interaction between BMI and age as well as sex and physical activity were performed, with only age revealing evidence ($P < 0.001$) for an interaction. Analyses including only validated cases and excluding cases with <2 years of follow-up time did not produce materially different results.

RESULTS

— The associations of BMI and risk of type 2 diabetes are presented in Table 1. Those considered to be normal weight (BMI 18.5–23.0 kg/m^2) had a 2.5-fold–increased risk of diabetes (HR 2.47 [95% CI 1.75–3.48]) compared with the referent category (BMI <18.5 kg/m^2). The HR increased with each successively increasing BMI category. Stratification by age produced similar trends across BMI but stronger associations in younger age-groups. In the analysis considering deciles (Table 2), participants in the second decile of BMI (18.8–20.2 kg/m^2) had an increased risk of diabetes with an HR of 1.70 (95% CI 1.20–2.42) compared with the lowest BMI decile. Risk across deciles increased monotonically ($P < 0.0001$). Furthermore, the trend and magnitude of risk across deciles held upon age stratification (data not presented). Analyses using alternative BMI cut points or the truncated

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Table 1—*HRs of type 2 diabetes by World Health Organization Southeast Asian cutoffs of BMI stratified by age*

		BMI			
	n	<18.5 kg/m^2 (*n* = 2,807)	18.5–23 kg/m^2 (*n* = 16,909)	23–27.5 kg/m^2 (*n* = 13,860)	>27.5 kg/m^2 (*n* = 3,515)
Incidence per 10,000 person-years follow-up		22	54	118	222
Women (cumulative incidence)	20,973	21 (1.4)	307 (3.2)	491 (6.5)	256 (11.8)
Men (cumulative incidence)	16,118	14 (1.1)	216 (3.0)	427 (6.8)	172 (12.8)
Full model		1.00	2.47 (1.75–3.48)	4.88 (3.48–6.85)	8.33 (5.88–11.79)
Age (years)					
<50	11,560	1.0	6.9 (1.7–27.9)	18.4 (4.6–74.0)	32.2 (7.9–130.7)
50–54	8,479	1.0	3.6 (1.6–8.0)	6.2 (2.7–13.9)	10.2 (4.4–23.4)
55–59	7,121	1.0	2.6 (1.2–5.5)	5.1 (2.4–10.9)	8.9 (4.1–19.4)
60–64	5,114	1.0	1.5 (0.8–2.8)	2.7 (1.5–4.8)	3.5 (1.9–6.5)
>65	4,817	1.0	2.0 (1.0–4.2)	3.3 (1.6–6.9)	7.0 (3.3–14.8)

Data are incidence and HR (95% CI). *Models are adjusted for age, sex, ethnicity, year of interview (1993–1995 and 1996–1998), hypertension (yes/no), smoking history (no, former, or current), education (none, primary, or secondary or more), alcohol intake (no, monthly, weekly, or daily), dietary factors (energy intake [kcal/day], fiber intake [g/day], total meat consumption [g/day], saturated fat [g/day], soft drink consumption [glasses/week], and coffee consumption [weekly, one, two, three, or four or more cups per day]), and moderate and strenuous physical activity in hours per week (moderate [e.g., walking] and strenuous [e.g., jogging]).

data (1st through 99th percentile) did not produce materially different results. The results from a nonparametric analysis are available in an online appendix (available at http://care.diabetesjournals.org/cgi/content/full/dc08-1674/DC1).

CONCLUSIONS — In this cohort of Chinese Singaporeans, risk of developing type 2 diabetes increased in BMIs considered lean and normal and continued in a dose-response fashion throughout the BMI range, with strong effect modification of BMI and diabetes risk by age. Our findings are consistent with a recent study suggesting that a BMI of ~21 kg/m^2 is an appropriate cutoff for obesity in Chinese and South Asian individuals based on parameters of glucose metabolism (5). Nonetheless, BMI cutoffs may be useful for population surveillance in the case of obesity and type 2 diabetes, but they do not appear to have strict biological meaning.

Few prospective studies have examined this question in Asians, and our data generally confirm the dose-response association observed in a couple populations (6,7); however, potentially important for public health approaches and clinicians, we report age-stratified results. Additionally, Singapore is highly prosperous and developed, potentially serving as a microcosm for other rapidly developing regions of Asia. Increasing evidence suggests that Asians have a relatively high susceptibility to type 2 diabetes based upon their anthropometry and how excess adiposity may affect insulin and glucose metabolism (8–11). These mechanisms are poorly understood, but it is theorized that excess body fat, especially visceral obesity, increases insulin resistance by releasing free fatty acids and cytokines that interfere with insulin action, along with other deleterious effects that could lead to diabetes (12). However, it appears unlikely that the metabolic burden of absolute adipose accumulation would be the mechanism driving diabetes risk at such low BMI ranges (19–21 kg/m^2) observed in the current study. Residual confounding by dietary and lifestyle factors, no assessment of family history of diabetes or other measures of adiposity, and the self-reported basis of BMI and diabetes in the study should also be considered as limits in interpreting the results.

In short, these findings demonstrate that risk of developing type 2 diabetes increases at low levels of BMI and continues to increase throughout the spectrum of BMI in Chinese Singaporeans. They also illustrate marked effect modification by age, as the association attenuated with increasing age. Continued and further research is needed to understand the association between adiposity and type 2 diabetes and to identify an optimal and healthful BMI range in Asians while considering diabetes and other health outcomes. With increasing obesity and diabetes rates in Asia, the development of public health approaches bringing awareness of and action to the issue has significant potential benefits.

Table 2—*HRs of type 2 diabetes by deciles of BMI in the Singapore Chinese Health Study*

Decile	*n*	Mean BMI (minimum–maximum)	HR (95% CI)
1	3,716	17.6 (11.6–18.8)	1.0
2	3,769	19.6 (18.8–20.2)	1.70 (1.20–2.42)
3	3,864	20.7 (20.2–21.1)	2.04 (1.45–2.85)
4	3,794	21.5 (21.1–21.9)	2.33 (1.68–3.25)
5	3,547	22.3 (21.9–22.7)	2.95 (2.14–4.07)
6	3,729	23.2 (22.7–23.5)	3.42 (2.49–4.68)
7	3,586	24.1 (23.5–24.5)	3.85 (2.82–5.26)
8	3,769	25.1 (24.5–25.7)	4.81 (3.55–6.52)
9	3,660	26.5 (25.7–27.3)	5.68 (4.20–7.68)
10	3,657	29.8 (27.4–68.9)	7.80 (5.80–10.48)

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