10.7603/s40602-014-0018-9

ASEAN Heart Journal
http://www.aseanheartjournal.org/

Vol. 22, no. 1, 122 – 129 (2014)
ISSN: 2315-4551

Original Article

Elevated cardiovascular risk factors in a young, asymptomatic and physically active population within a normal body mass index

Lee GK[1], Sim HW[1], Tan Y[1], Ma T[2], Liew KH[2], Tan EC[2], Lee LC[3], Sum CF[4], Ong HY[4]

[1]Department of Medicine (Drs. Lee GK, Sim HW, Tan Y) National University Health System, Singapore;
[2]Health for Life Program (Drs. Ma T, Liew KH, Tan EC) Khoo Teck Puat Hospital, Singapore;
[3]Gleneagles Hospital Penang, (Dr. Lee LC), Penang, Malaysia;
[4]Departments of Medicine (Dr. Sum CF) and Cardiology (Dr. Ong HY), Khoo Teck Puat Hospital, Singapore.

ABSTRACT

Background: Obesity is associated with significant morbidity and mortality. The body mass index (BMI) is a simple and inexpensive technique to quantify obesity. In a low-risk population, we aim to determine the association of BMI with cardiovascular risk factors (CVRFs) including undiagnosed diabetes.

Methods: We studied 3026 subjects referred for routine health screening. Patients with pre-existing diabetes mellitus and/or vascular disease were excluded. Each subject had anthropometric measurements and CVRF parameters (blood pressure, fasting lipids and fasting glucose) taken.

Results: The mean age was 38.9±5.4 years, 89.9% male. Chinese persons comprised 58.6% of our cohort, Malays 34.0% and Indians 7.4%. The majority (84.5%) of subjects were low-risk (10-year risk <10%) for cardiac events using the FRS algorithm. The mean BMI was 25.2kg/m². A positive correlation was seen between BMI and prevalence of CVRFs (p<0.001 for all). Serum lipid levels worsen significantly beyond a BMI of 20.0kg/m², while blood pressure worsens significantly beyond a BMI of 22.0kg/m². A positive relationship between BMI and the prevalence of impaired fasting glucose and frank diabetes was noted for BMIs ≥20.0kg/m² (p<0.001); no subject below 20.0kg/m² had frank diabetes.

Conclusion: A significant proportion of our subjects with a normal (Asian) BMI of <23.0kg/m² had elevated CVRFs on routine screening. The step-wise rise and additive nature of these CVRFs and her consistent correlation with a rising BMI of >20.0kg/m² suggest that traditional cardiovascular risk factors can be reduced to very low levels by weight reduction alone.

Keywords: body mass index, Asian, diabetes mellitus, hypertension, hyperlipidemia.

Running title: Increase in cardiovascular risk factors.

INTRODUCTION

Obesity refers to the accumulation of excess body fat to the extent that it has an adverse effect on health.[1] While it is contemporarily described as a disease of the developed world, it is now the sixth most important risk factor contributing to overall burden of disease worldwide.[2] It is one of the main preventable causes of morbidity and premature death,[3] yet it remains the most neglected public-health problem.[4] Its main adverse consequences are cardiovascular mortality, type 2 diabetes, and several cancers; it is also associated with a whole array of other medical and psychological problems such as hypertension, dyslipidemia, pulmonary diseases including obstructive sleep apnea, osteoarthritis, non-alcoholic steatohepatitis, gallbladder disease and depression.[1, 4]

The body mass index (BMI) is defined as weight in kilograms divided by the square of height in meters. It is a crude surrogate marker of body fat and does not take into account subjects with an increased BMI due to increased lean muscle mass; despite its shortcomings, it remains

Reprints: Dr. Ong HY, Department of Cardiology, Khoo Teck Puat Hospital, 90 Yishun Central, Singapore 768828, (65) 66023971
Email: ong.hean.yee@alexandrahealth.com.sg.

Published online: 19 December 2014

the most simple and common measure of excess body fat both in clinical practice and population surveys.[5] Analysis of the Framingham Heart Study participants has shown a correlation between obesity and risk for the development of cardiovascular risk factors, especially hypertension.[6]

For Western populations, based on the risk of developing diabetes and cardiovascular disease, the World Health Organization accepts a BMI of ≥25.0 kg/m² as abnormal; a BMI of 25.0 – 29.9 kg/m² is considered overweight and that ≥30.0 kg/m² is considered obese.[1] However, BMI cut points for South Asian and Chinese populations have been revised downwards; a BMI of 23.0 – 27.4 kg/m² already represents increased cardiovascular risk and that ≥27.5 kg/m² represents high cardiovascular risk.[7] The revision was necessitated by the strong evidence pointing to an increased risk of developing type 2 diabetes, hypertension and dyslipidemia amongst South Asian[8-11] and Chinese[12] subjects even at BMI levels of <25.0 kg/m², possibly due to a relative excess of adipose tissue or deficit of lean body mass compared with Europeans for a given BMI.[8, 13, 14] Studies on Singaporean subjects have demonstrated similar findings;[15, 16] in particular, a 70% and 104% increased risk of diabetes was noted for deciles with a mean BMI of only 19.6 and 20.7 kg/m² respectively.[17]

These studies are population-based cross-sectional studies encompassing a varied cohort of subjects, in terms of age, level of physical activity and comorbid conditions. We aim to determine the relationship between BMI and the prevalence of cardiovascular risk factors in a young, apparently healthy, asymptomatic and physically active population.

METHODS

Study sample and risk factor assessment

This is a retrospective cross-sectional study of 3026 Singaporeans in a physically active vocation from a single employer who were referred to our institution between April 2006 and July 2008 for employment-related health screening. Baseline demographics, smoking history, other co-morbidities (including type 2 diabetes, hypertension and dyslipidemia) and current medical treatment for all were obtained. Anthropometric measurements, office blood pressure, fasting glucose, and a lipid profile were taken for each subject.

The 10-year Framingham Risk Score (FRS) was calculated for each patient using information obtained from their demographic characteristics, history and fasting lipid profiles. The risk predictors used were age, total serum cholesterol, serum high-density lipoprotein (HDL), systolic blood pressure, treatment for hypertension (if any), and smoking status.[18] Low, moderate and high risk categories were defined as a 10-year risk for cardiac events of <10%, 10% – 19%, and ≥20% respectively.

Exclusions

Ninety-six subjects (3.2%) with pre-existing diabetes and/or vascular disease were excluded from the analysis.

Statistical analyses

The subjects were divided into 9 groups based on their BMI, with the first group corresponding to a BMI of <18.0 kg/m², the ninth corresponding to a BMI of ≥32.0 kg/m², and the others falling in between at equal intervals of 2 kg/m² apart. The mean systolic and diastolic blood pressures, total cholesterol, triglyceride, HDL and low-density lipoprotein (LDL) levels, cholesterol:HDL ratios, fasting glucose and FRS were computed for each BMI group. Further, the proportions of those with an adverse blood pressure, lipid, or fasting glucose profile were computed for each BMI group. The blood pressure profile was defined based on the criteria for pre-, stage 1 and 2 hypertension as set out by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure.[19] The lipid profile was defined in accordance with the Third Report of The National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III).[18] The definitions of impaired fasting glucose and frank diabetes were based on the criteria as defined by the 2003 Expert Committee on the Diagnosis and Classification of Diabetes Mellitus.[20]

The one-way ANOVA test with post hoc multiple comparisons and the χ^2 test were used to compare means and proportions between groups; a p-value of <0.05 indicated statistical significance. All analyses were performed using SPSS version 16.0 for Windows.

Institutional review board approval

The study was approved by the National Healthcare Group's Domain Specific Review Board (DSRB) (Study Number C/2011/00020).

RESULTS

The mean age was 38.9±5.4 years, 89.9% were males. Persons of Chinese descent comprised 58.6% of our cohort, Malays 34.0% and Indians 7.4%. The majority (84.5%) of subjects were low risk (10-year risk <10%) for cardiac events using the FRS algorithm. The mean BMI of our cohort was 25.2 kg/m and 71.8% and 24.9% of subjects had BMIs of over 23.0 and 27.5 kg/m² respectively. Figure 1 shows the correlation between BMI and systolic and diastolic blood pressure (p <0.001 for both) and figure 2 shows the correlation between BMI and total cholesterol, HDL levels, LDL levels and cholesterol:HDL ratios (p <0.001 for all). *Table 1* shows the proportions of subjects in each BMI group with an adverse blood pressure, lipid, or fasting glucose profile. Specifically, Figure 3 shows a positive relationship between BMI and the prevalence of impaired fasting glucose and frank diabetes mellitus was noted for BMIs ≥20.0 kg/m²; none of the subjects ≤20.0 kg/m² had frank diabetes. A strong positive correlation was noted between BMI and cardiovascular risk factors for BMIs ≥20.0 kg/m². Patients with BMI ≥20.0 kg/m² have increased odds of pre-hypertension and hypertension (OR 4.19, 95%CI 3.14 – 5.59), total cholesterol ≥5.2 mmol/L (OR 2.70, 95%CI 1.95 – 3.74), HDL <1.0 mmol/L (OR 4.90, 95%CI 2.00 – 12.04), LDL ≥3.4 mmol/L (OR 3.91, 95%CI 2.73 – 5.59), cholesterol:HDL ratio ≥4.5 (OR 9.41, 95%CI 5.08 – 17.46), abnormal fasting glucose (OR 2.05, 95%CI 1.03 – 4.06) and FRS ≥10% (OR 1.61, 95%CI 1.11 – 2.33) (p<0.001 for all except fasting glucose; p=0.036 and FRS; p=0.012).

DISCUSSION

Our data demonstrates the association between obesity and traditional cardiovascular risk factors in our population. While BMI cut points are useful as points for public health action, our findings remind us that the prevalence and severity of cardiovascular risk factors associated with obesity is not dichotomously defined. This applies even to the BMI band considered to be "normal" i.e. 18.5 – 23.0 kg/m². It should be noted that systolic blood pressure, total cholesterol and LDL begin to rise even at "normal" BMIs; the mean systolic blood pressure was considered at least pre-hypertensive (≥120 mmHg) and the mean total cholesterol and LDL levels considered at least borderline high (≥5.2 and ≥3.4 mmol/L respectively) for BMIs of ≥20.0 kg/m². Additionally, no subject with a BMI of <20.0 kg/m² had undiagnosed diabetes. Deurenberg-Yap et al showed that even at low categories of BMI of between 22.0 and 24.0 kg/m², the absolute risk for having at least one cardiovascular risk factor was high.[15, 16] Odegaard et al, using data from the Singapore Chinese Health Study, showed an increased risk of type 2 diabetes beginning at a "normal" BMI of 18.5 – 23.0 kg/m²,[17] Our data complements the findings in the other Singaporean studies as we have shown that blood pressure, lipids and diabetes status all share a strong positive relationship with BMI beginning at a low 18.0 – 20.0 kg/m² in our population.

Our finding that the majority of our relatively young cohort was classified low risk for cardiac events using the FRS algorithm is not totally unexpected. The FRS has been shown to classify young persons, perhaps inappropriately, as low risk because of its age-weighted nature.[21] Despite generally being classified as low risk, the risk factor burden in young patients presenting with an acute myocardial infarction is remarkably high.[22, 23] Young patients, particularly those with abnormal and even high-"normal" BMIs where cardiovascular risk factor burden is increased, may be inappropriately reassured on the basis of this classification.[23]

Our data is consistent with a study from Anqing, China, carried out in a predominantly rural and presumably physically active population which suggested a J-shaped relationship with CV risk factors starting at a BMI of <19.1 kg/m².[24] More recently, the Israeli Army's MELANY study showed that patients whose BMIs were well within the "normal" range in adolescence were also at risk of developing coronary artery disease in adulthood.[25] However, the Korean National Health Insurance Corporation study showed a U-shaped trend with a trough at a BMI of 23.0 – 24.9 kg/m² for systolic blood pressure, total cholesterol, fasting glucose and white cell count, but there was no indication that these differences were significant.[26]

While there is evidence that a "low-normal" BMI is associated with a reduction in cardiovascular risk factors, whether this translates into an association with mortality is controversial. Most large East Asian databases suggest a higher trough BMI for mortality. For example, the Chinese National Hypertension Survey showed a trough in mortality at a BMI of 24.0 – 24.9 kg/m²,[27] the Shanghai Diet and Cancer Study showed a trough in mortality at a BMI of 21.0 – 23.5 kg/m²,[28] and the Working Group on Obesity in China showing a J-shaped curve starting at a BMI of 24.0 kg/m² with respect to mortality.[29] Finally, a large meta-analysis of 19 cohorts in Asia showed a trough in mortality at a BMI of 22.6 – 27.5 kg/m² in East Asians but not in South Asians.[30] However, these studies could have been confounded by the presence of communicable disease and reduced access to medical care amongst those with a lower BMI given the heterogeneous composition of the populations in terms of age, socioeconomic status and non-cardiovascular mortality. Indeed, large proportions of the populations of India and China still inhabit rural regions[31] and have BMI values that are markedly lower than those observed in our cohort of Asians in an urbanized setting. For example, the mean BMI in the rural Anqing region of China is only 20.7 kg/m² in men and 20.9 kg/m² in women.[24]

On the other hand, the Korean Medical Insurance Study[32] showed that men with a BMI of <21.0 kg/m2 who maintained their BMI over time had a lower CVD mortality rates than those who intially had high BMIs or subsequently recorded increases in their BMI. The Singapore Chinese Health Study which included non-smoking Singaporean Chinese aged <65 years[33] showed a trough in mortality at a BMI of 18.5 – 21.4 kg/m². Despite the conflicting epidemiological evidence, Razak et al proposed to redefine obesity in these subjects with a BMI of ≥21.0 kg/m², yet at the same time acknowledging that such a cut point may seem unrealistic at least for an urbanized population.[5]

The differences in the optimal BMI ranges between Asian and Caucasian populations may be partially explained by the increased adiposity of Asians compared with Caucasians for a given BMI. Excess adiposity, especially visceral fat and regardless of BMI, is independently associated with increased cardiovascular risk.[34-36] Deurenberg-Yap et al noted that at any given body fat percentage the BMI of Singaporean subjects was about 3.0kg/m² lower than that of Caucasians.[15] Therefore, given their relative excess of adipose tissue even at normal BMI levels, the independent cardiovascular risk that excess adiposity imposes may be applicable to South Asian and Chinese subjects even if they were within traditional BMI cut-off points.

As the vast majority of our study cohort was from a single employer, they were relatively uniform in terms of age, educational level, access to public health care and physical activity, minimizing some of the confounders that may have been present in other population-based studies. Nonetheless, our study does have its limitations. The cross-sectional nature of our study permits only a single encounter with each subject. It also allows us only a single measurement of blood pressure and other biochemical parameters, resulting in the possibility of false readings especially for blood pressure. It does not permit follow-up to determine the relationship between BMI (or change in BMI) and other endpoints such as coronary artery disease, acute coronary syndrome and mortality. Prospective follow-up of this cohort may be useful to validate the relationship between BMI and morbidity or mortality. We also did not perform an oral glucose tolerance test, which may be more sensitive in detecting diabetes and pre-diabetic states. The numbers of patients at the extreme ends of the BMI spectrum were also small, rendering us unable to conclusively analyze risk factor burden in these groups of subjects. The numbers of subjects in each ethnic group were also too small to analyse individually.

CONCLUSION

Although mean values of cardiovascular risk factors generally remained within established Western guidelines for low risk subjects in our study, we demonstrated a step-wise rise and cumulative increase in cardiovascular risk factors with a rising BMI beginning at 20.0 kg/m². Our study lends weight to the evidence that, everything else being equal, traditional cardiovascular risk factors can be reduced to very low levels by weight reduction alone. Further large-scale epidemiological studies that are adjusted for exercise, educational levels, socio-economic status and access to healthcare amongst their subjects are required to further delineate the ideal BMI range that is associated with a reduced mortality.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

Figure 1. The relationship between BMI and systolic and diastolic blood pressure.

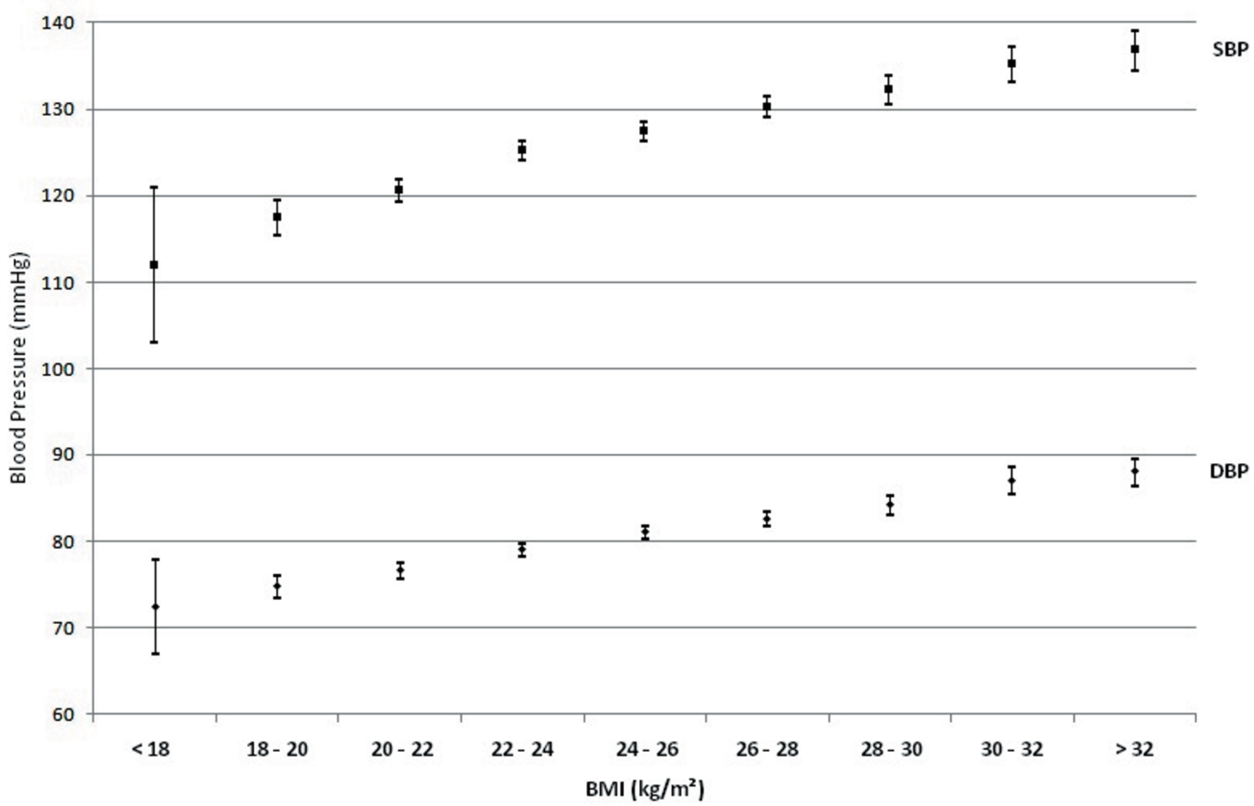

Figure 2. The relationship between BMI and cholesterol parameters.

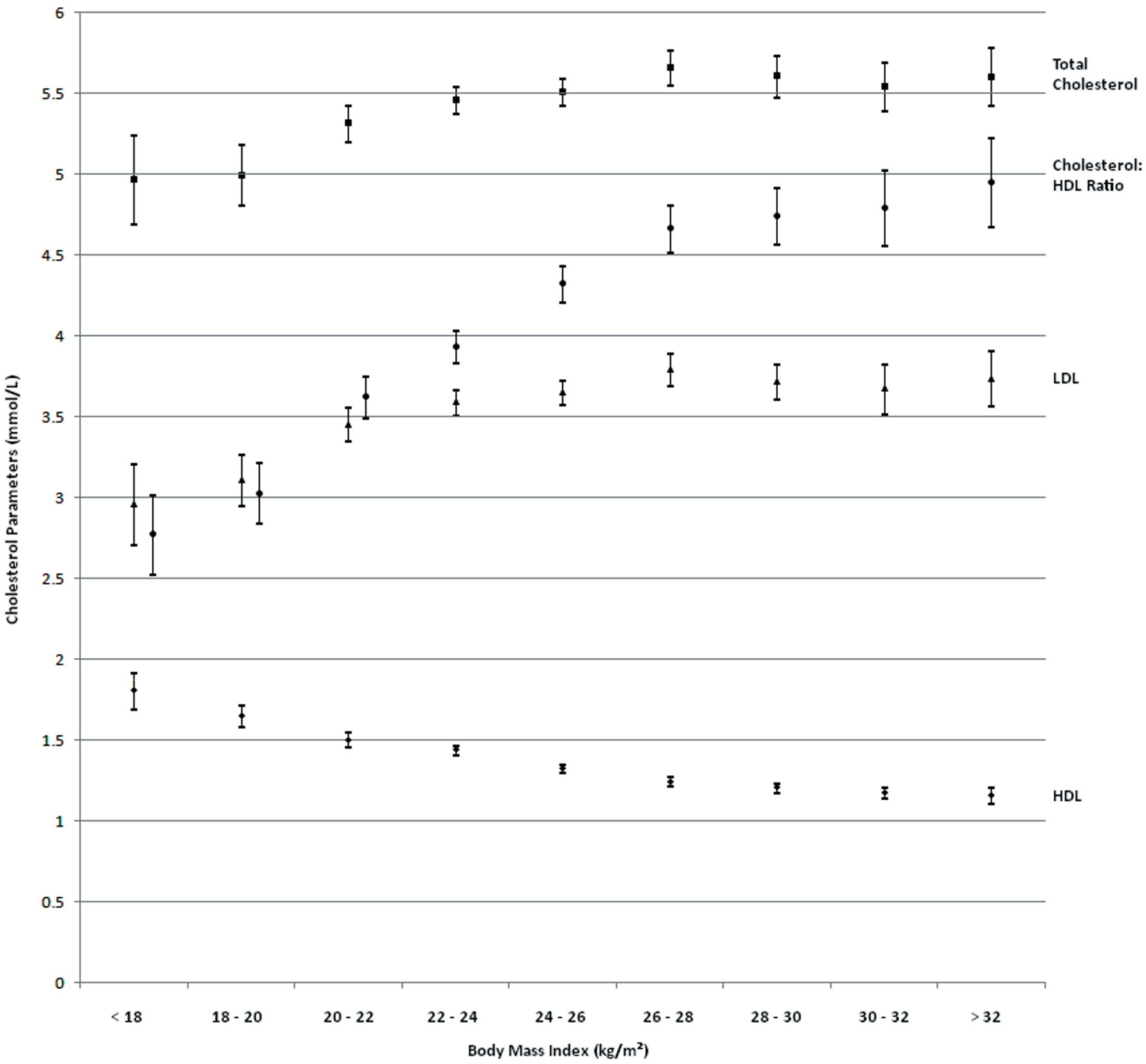

Figure 3. The relationship between BMI and impaired fasting glucose and frank diabetes mellitus.

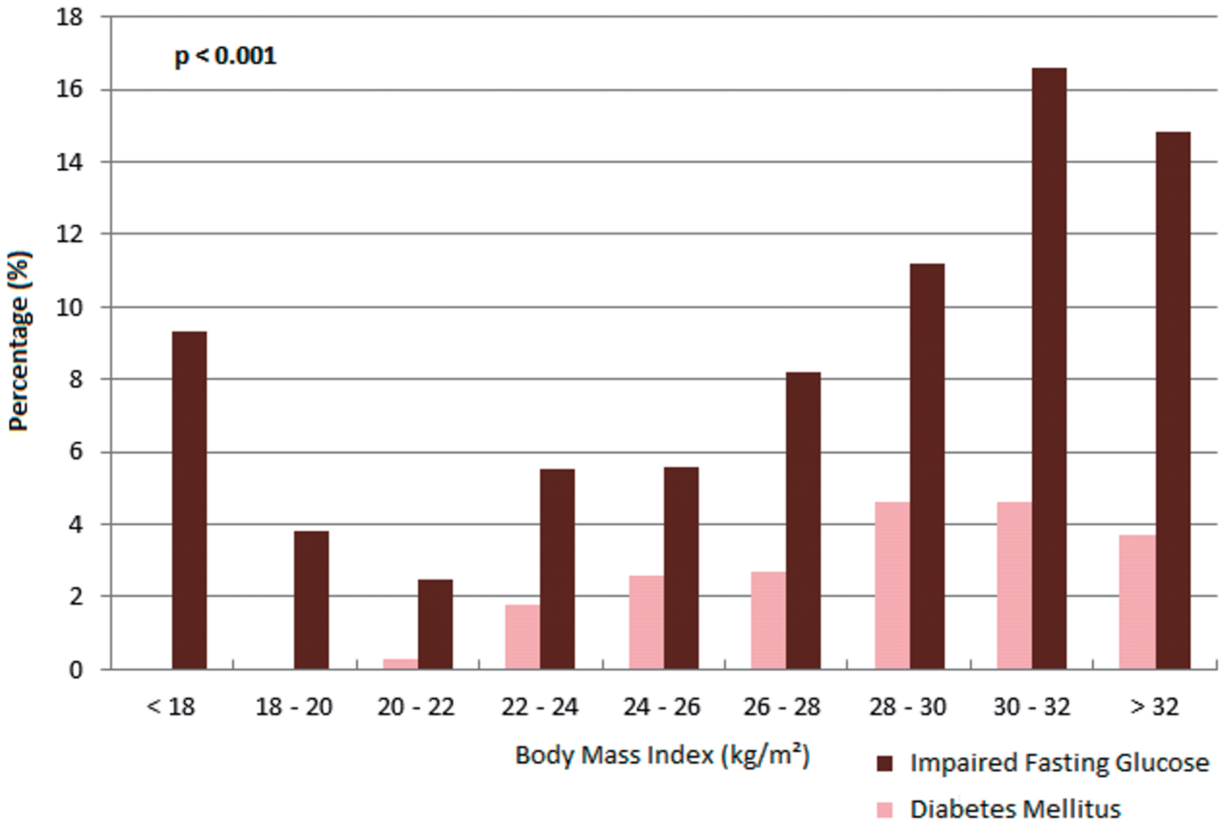

Table 1. Proportions of subjects in each BMI group with an adverse blood pressure, lipid, or fasting glucose profile.

Risk Factor	Body Mass Index (kg/m²)									p-value*
	< 18	18 – 20	20 – 22	22 – 24	24 – 26	26 – 28	28 – 30	30 – 32	≥ 32	
n	**50**	**158**	**369**	**618**	**679**	**492**	**323**	**183**	**154**	
Blood Pressure										<0.001
Normal	51.1%	50.6%	42.0%	26.4%	18.9%	11.0%	10.2%	8.2%	5.2%	
Pre-HTN	36.2%	41.8%	46.9%	57.0%	57.8%	60.0%	52.9%	45.4%	42.9%	
Stage 1 HTN	10.6%	7.0%	10.8%	13.3%	19.0%	24.6%	27.2%	32.8%	35.1%	
Stage 2 HTN	2.1%	0.6%	0.3%	3.4%	4.3%	4.5%	9.6%	13.7%	16.9%	
Total Cholesterol (mmol/L)										<0.001
< 5.2	65.9%	65.1%	49.7%	43.1%	40.5%	37.2%	40.2%	36.5%	35.1%	
5.2 – 6.1	24.4%	24.8%	33.7%	36.1%	35.7%	33.7%	33.5%	40.9%	38.8%	
≥ 6.2	9.8%	10.1%	16.7%	20.9%	23.8%	29.2%	26.3%	22.6%	26.1%	
HDL (mmol/L)										<0.001
≥ 1.6	65.0%	50.4%	36.9%	27.7%	15.9%	10.2%	9.0%	4.0%	6.1%	
1.0 – 1.5	35.0%	45.5%	57.0%	66.2%	72.6%	71.6%	69.1%	75.8%	67.4%	
< 1.0	0.0%	4.1%	6.1%	6.1%	11.5%	18.2%	21.9%	20.1%	26.5%	
LDL (mmol/L)										<0.001
< 2.6	37.5%	28.5%	14.7%	12.5%	11.9%	7.8%	8.3%	10.1%	13.6%	
2.6 – 3.3	40.0%	43.9%	36.6%	32.4%	28.2%	30.3%	32.0%	27.5%	18.9%	
3.4 – 4.0	12.5%	13.8%	27.7%	27.5%	30.1%	27.9%	29.2%	32.2%	30.3%	
≥ 4.1	10.0%	13.8%	20.9%	27.7%	29.9%	33.9%	30.4%	30.2%	37.1%	
Cholesterol:HDL Ratio										<0.001
< 4.5	100.0%	91.1%	81.5%	71.7%	59.1%	48.4%	46.5%	44.3%	41.7%	
≥ 4.5	0.0%	8.9%	18.5%	28.3%	40.9%	51.6%	53.5%	55.7%	58.3%	
Fasting Glucose										<0.001
Normal	90.7%	96.2%	97.2%	92.7%	91.8%	89.1%	84.2%	78.8%	81.5%	
IFG	9.3%	3.8%	2.5%	5.5%	5.6%	8.2%	11.2%	16.6%	14.8%	
Diabetes	0.0%	0.0%	0.3%	1.8%	2.6%	2.7%	4.6%	4.6%	3.7%	
Framingham Risk Score										0.370 (NS)
< 10%	91.7%	87.2%	87.9%	84.4%	83.7%	82.2%	85.7%	79.9%	83.2%	
10 – 19%	6.2%	7.1%	8.6%	12.2%	10.9%	13.0%	10.3%	12.9%	14.3%	
≥ 20%	2.1%	5.7%	3.5%	3.4%	5.4%	4.8%	4.0%	7.2%	2.5%	

*The χ^2 test was used to compare proportions between each BMI group; a p-value of <0.05 indicated statistical significance.

REFERENCES

1. **Haslam DW,** James WP. Obesity. *Lancet.* Oct 1 2005;366(9492):1197-1209.

2. **Ezzati M,** Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ. Selected major risk factors and global and regional burden of disease. *Lancet.* Nov 2 2002;360(9343):1347-1360.

3. **Mokdad AH,** Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. JAMA. Mar 10 2004;291(10):1238-1245.

4. **Obesity:** preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser.* 2000;894:i-xii, 1-253.

5. **Razak F,** Anand SS, Shannon H, *et al.* Defining obesity cut points in a multiethnic population. *Circulation.* Apr 24 2007;115(16):2111-2118.

6. **Wilson PW,** D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Arch Intern Med.* Sep 9 2002;162(16):1867-1872.

7. **Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies.** *Lancet.* Jan 10 2004;363(9403):157-163.

8. **Forouhi NG,** Jenkinson G, Thomas EL, et al. Relation of triglyceride stores in skeletal muscle cells to central obesity and insulin sensitivity in European and South Asian men. *Diabetologia.* Aug 1999;42(8):932-935.

9. **Jafar TH,** Chaturvedi N, Pappas G. Prevalence of overweight and obesity and their association with hypertension and diabetes mellitus in an Indo-Asian population. *CMAJ.* Oct 24 2006;175(9):1071-1077.

10. **Lear SA,** Toma M, Birmingham CL, Frohlich JJ. Modification of the relationship between simple anthropometric indices and risk factors by ethnic background. *Metabolism.* Oct 2003;52(10):1295-1301.

11. **Lovegrove JA,** Brady LM, Lesauvage SV, Lovegrove SS, Minihane AM, Williams CM. Lack of association between central adiposity and lipaemia in UK Sikh men. *Int J Obes Relat Metab Disord.* Nov 2003;27(11):1373-1382.

12. **Unwin N, Harland J,** White M, *et al.* Body mass index, waist circumference, waist-hip ratio, and glucose intolerance in Chinese and Europid adults in Newcastle, UK. J Epidemiol Community Health. Apr 1997;51(2):160-166.

13. **Chang CJ,** Wu CH, Chang CS, *et al.* Low body mass index but high percent body fat in Taiwanese subjects: implications of obesity cutoffs. *Int J Obes Relat Metab Disord.* Feb 2003;27(2):253-259.

14. **Chowdhury B,** Lantz H, Sjostrom L. Computed tomography-determined body composition in relation to cardiovascular risk factors in Indian and matched Swedish males. *Metabolism.* May 1996;45(5):634-644.

15. **Deurenberg-Yap M,** Chew SK, Deurenberg P. Elevated body fat percentage and cardiovascular risks at low body mass index levels among Singaporean Chinese, Malays and Indians. O*bes Rev.* Aug 2002;3(3):209-215.

16. **Deurenberg-Yap M,** Chew SK, Lin VF, Tan BY, van Staveren WA, Deurenberg P. Relationships between indices of obesity and its co-morbidities in multi-ethnic Singapore. *Int J Obes Relat Metab Disord.* Oct 2001;25(10):1554-1562.

17. **Odegaard AO,** Koh WP, Vazquez G, *et al.* BMI and diabetes risk in Singaporean Chinese. *Diabetes Care.* Jun 2009;32(6):1104-1106.

18. **Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection,** Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* May 16 2001;285(19):2486-2497.

19. **Chobanian AV,** Bakris GL, Black HR, *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA.* May 21 2003;289(19):2560-2572.

20. **Genuth S,** Alberti KG, Bennett P, *et al.* Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care.* Nov 2003;26(11):3160-3167.

21. **Wilson PW,** D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation.* May 12 1998;97(18):1837-1847.

22. **Zarich S,** Luciano C, Hulford J, Abdullah A. Prevalence of metabolic syndrome in young patients with acute MI: does the Framingham Risk Score underestimate cardiovascular risk in this population? *Diab Vasc Dis Res.* Sep 2006;3(2):103-107.

23. **Lee GK,** Lee LC, Liu CW, *et al.* Framingham risk score inadequately predicts cardiac risk in young patients presenting with a first myocardial infarction. *Ann Acad Med Singapore.* Mar 2010;39(3):163-167.

24. **Hu FB,** Wang B, Chen C, *et al.* Body mass index and cardiovascular risk factors in a rural Chinese population. Am J Epidemiol. Jan 1 2000;151(1):88-97.

25. **Tirosh A,** Shai I, Afek A, *et al.* Adolescent BMI trajectory and risk of diabetes versus coronary disease. *N Engl J Med.* Apr 7 2011;364(14):1315-1325.

26. **Jee SH,** Sull JW, Park J, *et al.* Body-mass index and mortality in Korean men and women. *N Engl J Med.* Aug 24 2006;355(8):779-787.

27. **Gu D,** He J, Duan X, *et al.* Body weight and mortality among men and women in China. *JAMA.* Feb 15 2006;295(7):776-783.

28. **Yuan JM,** Ross RK, Gao YT, Yu MC. Body weight and mortality: a prospective evaluation in a cohort of middle-aged men in Shanghai, China. *Int J Epidemiol.* Oct 1998;27(5):824-832.

29. **Zhou BF.** Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults. *Biomed Environ Sci.* Sep 2002;15(3):245-252.

30. **Zheng W,** McLerran DF, Rolland B, *et al.* Association between body-mass index and risk of death in more than 1 million Asians. *N Engl J Med.* Feb 24 2011;364(8):719-729.

31. **Human Development Report 2001.** New York, NY: Oxford University Press; 2001.

32. **Yun KE,** Park HS, Song YM, Cho SI. Increases in body mass index over a 7-year period and risk of cause-specific mortality in Korean men. Int J Epidemiol. Apr 2010;39(2):520-528.

33. **Odegaard AO,** Pereira MA, Koh WP, *et al.* BMI, all-cause and cause-specific mortality in Chinese Singaporean men and women: the Singapore Chinese health study. *PLoS One.* 2010;5(11):e14000.

34. **Hubert HB,** Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation.* May 1983;67(5):968-977.

35. **Sowers JR.** Obesity as a cardiovascular risk factor. *Am J Med.* Dec 8 2003;115 Suppl 8A:37S-41S.

36. **Van Gaal LF,** Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. *Nature.* Dec 14 2006;444(7121):875-880.