Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 62–67

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Frequency of insulin resistance in nondiabetic adult Bangladeshi individuals of different obesity phenotypes

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ARTICLE INFO

Article history:
Received 24 July 2018
Accepted 21 August 2018

Keywords:
Insulin resistance
Nondiabetic adult
Metabolic syndrome
Metabolic obesity
Obesity phenotypes

ABSTRACT

Insulin resistance (IR) is the corner stone of metabolic obesity. This cross-sectional analytical study was aimed to find out the frequency of IR in non-diabetic adult individuals of different obesity phenotypes that would help to implement preventive measures to avoid the cardiometabolic catastrophes.

Methods: Total 955 nondiabetic adult individuals were selected and categorized into six metabolic phenotypes by metabolic syndrome criteria in each BMI group (18.5–24.9-normal weight, 25-29.9-overweight, ≥30-obese). From them, metabolically obese normal weight, metabolically obese overweight, metabolically healthy obese and metabolically unhealthy obese were selected as Obesity phenotypes (N = 616).

Results: The frequency of IR was found to be very high (60.2%) in total nondiabetic adult obese individuals (N = 616). Highest frequency of IR was found in MUO phenotype (76.3%), lowest frequency of IR was found in MONW phenotype (37.1%) and frequency of IR in MOOW and MHO phenotypes found to be identical but significantly ($p < 0.0001$) less than MUO and significantly ($p < 0.0001$) more than MONW phenotype. Among the obesity phenotypes, females were more insulin resistant than males (67.5% vs 48.1% respectively, $p < 0.05$). Frequency of IR found significantly ($p < 0.05$) more in female than male in all obesity phenotypes except in MUO phenotype where males found to show significantly ($p < 0.05$) higher frequency than females. Frequency of IR was significantly higher in younger (20–39 yrs) age group than 40–60 yrs age group (63.2% vs 53.5% respectively, $p < 0.05$).

Conclusion: IR is alarmingly high (60.2%) in nondiabetic adult obese individuals. Among different obesity phenotypes, it is highest (76.3%) in MUO and lowest (37.1%) in MONW.

1. Introduction

Worldwide prevalence of overweight and obesity is increasing day by day which are frequently associated with increased risk of morbidity (like diabetes, cardiovascular disease etc.) and mortality [1,2]. BMI based classification is simple but do not adequately reflect adiposity [3,4]. Overweight and obese individuals may have no cardiometabolic risk, whereas normal weight individuals may present with cardiometabolic risk [5,6].

The term “Metabolic Obesity” has been floated to resolve this issue [7]. Metabolic obesity stands for the individual with unhealthy metabolic health (metabolic profile). Unhealthy metabolic health is featured by metabolic syndrome (MetS) irrespective of BMI. On the other hand, healthy metabolic health indicates absence of MetS irrespective of BMI [7,8].

Different studies [8,9] brought out the metabolically unhealthy and healthy phenotypes in different BMI groups (18.5–24.9-normal weight, 25-29.9-overweight, ≥30-obese) [10] on the basis of presence or absence of MetS respectively. Individuals having 0–2

Abbreviations: BSMMU, Bangabandhu Sheikh Mujib Medical University; BMI, body mass index; IR, Insulin resistance; HDL-C, high density lipoprotein-cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; MHNW, metabolically healthy normal weight; MHO, metabolically healthy obese; MHOW, metabolically healthy overweight; MONW, metabolically obese normal weight; MOOW, metabolically obese overweight; MUO, metabolically unhealthy obese; MetS, metabolic syndrome; NCEP ATP III criteria, National Cholesterol Education Program Adult Treatment Panel III; OPD, outpatient department.

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https://doi.org/10.1016/j.dsx.2018.08.022
1871-4021/

components of MetS and ≥3 components of MetS were considered 'metabolically healthy & metabolically unhealthy' respectively. Metabolic obesity represents the metabolically unhealthy status of an individual irrespective of their BMI. Therefore, in different BMI groups finally they addressed six metabolic phenotypes; metabolically healthy normal weight (MHNW), metabolically obese normal weight (MONW), metabolically healthy overweight (MHOW), metabolically obese overweight (MOOW), metabolically healthy obese (MHO) and metabolically unhealthy obese (MUO). Out of these six metabolic phenotypes, MONW, MOOW, MHO and MUO are regarded as 'Obesity phenotypes' [8,9].

Although, many different definitions are used for metabolic health, insulin resistance (IR) is the focal point of metabolic obesity [11] and adipose tissue dysfunction is the corner stone of IR [12,13]. In obese individuals, adipose tissue releases increased amounts of non-esterified fatty acids, glycerol, hormones, pro-inflammatory cytokines and other factors that are involved in the development of IR. When IR is accompanied by dysfunction of pancreatic islet β-cells, it results in poor glycemic control and ultimately leads to development of type 2 diabetes [14]. Therefore, the burdens of IR in different obesity phenotypes of different BMI groups need to be explored to identify individuals at high risk of developing diabetes. However, to the best of our knowledge, no study has previously done on Bangladeshi population regarding this issue.

Furthermore, Bangladeshi peoples are at high risk of developing type 2 diabetes because of some facts like more propensity to abdominal obesity, higher visceral or subcutaneous fat despite lower waist circumference or BMI. The present study was aimed to find out the frequency of insulin resistance among nondiabetic adult individuals of different obesity phenotypes and to give a comprehensive view of IR among nondiabetics which would raise awareness about IR to them and help to implement preventive measures on insulin resistant populations to avoid their shift to overt diabetes mellitus.

2. Materials and methods

2.1. Study subjects

With approval of protocol by Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (BSMMU), a population based cross sectional analytical study was performed from March 2016 to February 2017. Both male and female subjects aged 20–60 years with BMI ≥18.5 were included and subjects with diabetes mellitus, stroke, cancer, chronic diseases & pregnancy were excluded. By convenient and purposive sampling, total 1000 adult individuals with their healthy attendants were selected from BSMMU outpatient department (OPD) according to inclusion and exclusion criteria. Finally we enrolled 955 nondiabetic adult individuals. 45 individuals with fasting blood glucose ≥7.0 mmol/L, triglyceride levels >400 mg/dL were excluded.

The study subjects were divided into different body mass index (BMI) groups and then categorized into metabolically healthy and unhealthy phenotypes by metabolic syndrome (MetS) criteria in each BMI group (18.5–24.9-normal weight, 25-29.9-overweight, ≥30-obese). So, ultimately all the study subjects were categorized into six metabolic phenotypes: metabolically healthy normal weight (MHNW), metabolically obese normal weight (MONW), metabolically healthy overweight (MHOW), metabolically obese overweight (MOOW), metabolically healthy obese (MHO) & metabolically unhealthy obese (MUO). From them metabolically obese normal weight (MONW), metabolically obese overweight (MOOW), metabolically healthy obese (MHO) & metabolically unhealthy obese (MUO) were selected as Obesity phenotypes (N = 616).

2.2. Measurements

All subjects were briefed about the study properly & after taking written informed consents, their demographic profile and BP, anthropometric parameters including height, weight, waist circumference and hip circumference were measured & recorded in a preformed data sheet. Weight and height were measured with the subjects in the standing position, in light clothing and without shoes using a fixed scale with stadiometer. Waist circumference was measured in centimeter by a measuring tape while the subjects were in a standing position. The anatomical landmarks used for this measurement were midway between the lowest portion of the rib cage and iliac crest laterally and the umbilicus anteriorly. BMI was calculated as weight (kg) divided by height (m^2).

2.3. Laboratory assays

With full aseptic precaution, fasting blood samples were collected after an overnight fasting of >12 h from all subjects and measured in the Department of Biochemistry & Molecular Biology, BSMMU. Fasting glucose was measured by hexokinase method (ARCHITECT ci4100, USA) whereas, fasting serum insulin was measured by microparticle enzyme immunoassay (MEIA) (ARCHITECT ci4100, USA). Fasting serum HDL-C was measured by enzymatic color test and serum triglyceride was measured by enzymatic glycerol phosphate oxidase method (Beckman Coulter Inc., USA).

2.4. Operational definitions

HOMA-IR: Fasting insulin (μU/mL) × FPG (mmol/L)/22.5 [15].

Insulin resistance: HOMA-IR ≥2.8 was considered on the basis of previous studies which is the value that better predicts the developing of diabetes and correlates with the gold standard diagnostic method of IR: hyperglycemic–hyperinsulinemic clamp test [16–20] as there is no well-agreed recommended cutoff value as yet in Bangladesh.

Metabolic syndrome (MetS): It was defined as the presence of ≥3 of the following 5 components according to NCEP-ATP III, 2005 revision [21]:

a. Waist circumference (≥102 cm in men, ≥88 cm in women).
b. Plasma triglyceride ≥150 mg% or on drug treatment.
c. Plasma HDL-C <40 mg% in men, <50 mg% in women or on drug treatment.
d. Hypertension (systolic ≥130 mmHg &/or diastolic ≥85 mmHg or on antihypertensive drug treatment.
e. Fasting blood glucose ≥100 mg% or on drug treatment.

2.5. Statistical analysis

Collected data were entered, checked, edited and then processed with the help of the software Statistical Package for Social Sciences (SPSS) version 22.0. Results were expressed as mean ± SD for quantitative data and as absolute or relative frequencies for qualitative data. Differences between the groups were analyzed by one-way ANOVA followed by Bonferroni post-hoc test. Frequency of obesity phenotypes, IR were determined at 95% confidence interval (CI) and compared among different obesity phenotypes by Chi-square test and two sample proportion test as adequate. A value of $p < 0.05$ was considered as statistically significant.

3. Results

Initially, we recruited 955 nondiabetic adult individuals attending BSMMU OPD. Among them, MOOW, MUO & MHOW phenotypes found to predominate (supplementary Table I). Finally, we enrolled 616 nondiabetic adult obese individuals in our study. Among them, MOOW & MUO phenotypes found to predominate with lowest frequency in MONW phenotype (Table 1).

As shown in Table 2, frequency of insulin resistance was found significantly very high (60.2%) in 616 metabolically obese nondiabetic adult individuals compared to metabolically nonobese group (n = 339).

In Table 3, observing the frequency of IR among different obesity phenotypes of nondiabetic adult obese individuals, we found highest frequency of IR (76.3%) in MUO phenotype & lowest frequency of IR (37.1%) in MONW phenotype with statistical significance. Frequency of IR in MOOW & MHO phenotypes found to be identical but significantly less than MUO and significantly more than MONW phenotype.

However, as shown in Table 4, frequency of IR between different age groups of 616 nondiabetic adult obese individuals were compared and found significantly high in younger (20–39 y) age group which was 63.2%. Moreover, females were more insulin resistant than males (67.5% vs 48.1%, $p < 0.05$) among the total obesity phenotypes (n = 616). (Table 4).

Furthermore, frequency of IR found significantly ($p < 0.05$) more in female than male in all obesity phenotypes except in MUO phenotype where males found to show significantly ($p < 0.05$) higher frequency than females (Table 5).

4. Discussion

In this study, we used NCEP-ATP III criteria of MetS [21] to identify metabolically healthy and unhealthy phenotypes. From the initial recruitment of 955 nondiabetic adults, finally we enrolled 616 individuals of different obesity phenotypes in our study. Among them, MOOW & MUO phenotypes were found to predominate (41.4% and 35.6% respectively) with lowest frequency in MONW phenotype (10.1%). This data is supported by different studies [8,22]. A Finland study [8] on general population aged 45–74 years found the prevalence of obesity phenotypes as follows; MOOW (47.2%), MUO (35.4%), MONW (11.9%), MHO (5.5%) by using Harmonization definition of MetS [22]. Another study found this prevalence among US population as follows; MUO (37.5%), MOOW (30.5%), MHO (17.4%) & MONW (14.5%) by defining metabolic health using six cardiometabolic components [23].

In our study, the frequency of insulin resistance (IR) was found to be very high (60.2%) in total nondiabetic adult obese individuals (N = 616). A cross sectional study on nondiabetic Chinese adults (median BMI = 24.4) found the frequency of IR in nondiabetics 36.7% [24]. Another study on 511 nondiabetic Taiwanese adults (median BMI = 26.5) found this frequency 20.7% [25]. In addition, previous studies also revealed that Asian Indians are more insulin resistant than Caucasians, independent of their generalized or truncal adiposity [26,27].

However, to our knowledge, previous studies were done on apparently healthy nondiabetic individuals. But, our study subjects were nondiabetic adult obese individuals; who were obese either metabolically or phenotypically. In obese individual, adipose tissue releases increased amounts of non-esterified fatty acids, glycerol, hormones, pro-inflammatory cytokines and other factors that are involved in the development of IR [12]. As IR is associated with obesity, therefore, we found frequency of insulin resistance significantly high in metabolically obese nondiabetic adult individuals than metabolically nonobese individuals.

Comparing the frequency of insulin resistance among different obesity phenotypes, we found highest frequency in MUO phenotype (76.3%), lowest frequency in MONW phenotype (37.1%) & frequency of IR in MOOW & MHO phenotypes found to be identical but significantly less than MUO and significantly more than MONW phenotype. Our results showed progressively increasing IR in higher BMI groups. This finding is consistent with finding of a previous study that conducted on 314 nondiabetic, normotensive healthy individuals and found BMI and insulin resistance positively correlated ($r = 0.456$, $p < 0.001$) and finally, concluded that the greater the BMI, the more the insulin resistant individual [28].

However, frequency of IR in MOOW & MHO phenotypes found to be identical possibly because of high adiponectin level in MHO phenotype. Adiponectin concentrations usually remain high in metabolically healthy phenotype (e.g. MHNW, MHO etc.) than metabolically unhealthy phenotype (e.g. MOOW) [29]. Adiponectin is an insulin sensitizing, antiatherogenic and anti-inflammatory agent [30]. Hence, frequency of IR in MHO found low to be identical with that of MOOW phenotype. A recent study

Table 1
Baseline characteristics of different obesity phenotypes (N = 616).

Variables	Metabolically obese normal weight (MONW)	Metabolically obese overweight (MOOW)	Metabolically healthy obese (MHO)	Metabolically unhealthy obese (MUO)
n (%)	62 (10.1)	255 (41.4)	80 (13)	219 (35.6)
Male/female (n)	44/18[d]	117/138[d]	21/59[d]	49/170[d]
Age (years)	38.3 ± 8.9	38.5 ± 7.9	33.7 ± 7.4[a]	35.9 ± 8.3[ab]
BMI (Kg/m^2)	23.6 ± 1.2	27.7 ± 1.3[a]	33.3 ± 2.6[ab]	33.7 ± 3.3[ab]
Waist circumference (cm)	87.6 ± 4.9	94.3 ± 5.5[a]	101 ± 7.4[ab]	102.8 ± 9[ab]
Serum HDL-C (mg%)	39.9 ± 7.2	37.3 ± 7.1[a]	40.8 ± 8.5[bc]	36.3 ± 7.9[a]
Serum triglyceride (mg%)	227.7 ± 120.8	201.1 ± 87.6	117.9 ± 44.4[abc]	180.9 ± 83.7[a]
Fasting glucose (mmol/L)	5.3 ± 0.7	5.3 ± 0.6	4.8 ± 0.5[abc]	5.3 ± 0.6
Fasting insulin (μU/mL)	11.1 ± 4.9	14.2 ± 6.7[a]	15.7 ± 7.4[a]	16.8 ± 6.8[ab]
HOMA-IR	2.7 ± 1.4	3.3 ± 1.8[a]	3.3 ± 1.5[c]	3.5 ± 1.8[ab]

Continuous variables are reported as mean ± SD and one-way ANOVA followed by Bonferroni post-hoc test was done to find out the level of significance. Categorical variables are reported as absolute or relative frequencies and analyzed by Chi-Square test.
[a] $p < 0.05$ between MONW & others (MOOW, MHO, MUO).
[b] $p < 0.05$ between MOOW & others (MHO, MUO).
[c] $p < 0.05$ between MHO & MUO.
[d] $p < 0.05$ between male & female.

Table 2
Comparison of frequency of insulin resistance between metabolically obese and metabolically nonobese nondiabetic adult individuals (N = 955).

Total nondiabetic adult individuals N = 955	Insulin resistance (HOMA-IR ≥2.8) N = 500	Percent	95%CI	*P* value
Metabolically obese (n = 616)	371	60.2	56.2–64	<0.05
Metabolically nonobese (n = 339)	129	39.8	34.5–45.1	

HOMA-IR=Homeostatic model assessment of insulin resistance.
Two sample proportion test was done to find out the level of significance.

Table 3
Comparison of frequency of insulin resistance among different obesity phenotypes of nondiabetic adult obese individuals.

Obesity phenotypes n = 616	IR present (HOMA-IR ≥2.8) n = 371	IR absent (HOMA-IR <2.8) n = 245	*p* value
MONW (n = 62)	23 (37.1%)	39 (62.9%)	0.000
MOOW (n = 255)	138 (54.1%)	117 (45.9%)	
MHO (n = 80)	43 (53.8%)	37 (46.3%)	
MUO (n = 219)	167 (76.3%)	52 (23.7%)	

Chi-Square test was done to find out the level of significance. MONW = Metabolically obese normal weight, MOOW = Metabolically obese overweight, MHO = Metabolically healthy obese and MUO = Metabolically unhealthy obese.

Obesity phenotypes	*p* value
MONW vs MOOW	<0.05
MONW vs MHO	<0.05
MONW vs MUO	<0.05
MOOW vs MHO	>0.05
MOOW vs MUO	<0.05
MHO vs MUO	<0.05

Two sample proportion test was done to find out the level of significance.
MONW = Metabolically obese normal weight, MOOW = Metabolically obese overweight.
MHO = Metabolically healthy obese and MUO = Metabolically unhealthy obese.

Table 4
Comparison of frequency of insulin resistance between gender & different age groups of nondiabetic adult obese individuals (N = 616).

Total subjects (N = 616)	Insulin resistance N = 371	%	*p* value
Age group[a] (20–39 yrs/40–60 yrs; n = 429/187)	271/100	63.2/53.5	<0.05
Male/female (n = 231/385)	111/260	48.1/67.5	<0.05

Two sample proportion test was done to find out the level of significance.
[a] Age grouping was done based on a conventional concept that type 2 DM is commonly seen in subjects with age 40 yrs or more who have high propensity to develop IR.

Table 5
Comparison of frequency of insulin resistance (IR) between male and female in different obesity phenotypes.

Obesity phenotypes n = 616	Male n = 231			Female n = 385			*p* value
	Phenotype total	IR n = 111	%	Phenotype total	IR n = 260	%	
MONW (n = 62)	44	14	31.8	18	9	50	<0.05
MOOW (n = 255)	117	49	41.9	138	89	64.5	<0.05
MHO (n = 80)	21	9	42.9	59	34	57.6	<0.05
MUO (n = 219)	49	39	79.6	170	128	75.3	<0.05

Two sample proportion test was done to find out the level of significance.
MONW = Metabolically obese normal weight, MOOW = Metabolically obese overweight, MHO = Metabolically healthy obese and MUO = Metabolically unhealthy obese.

revealed that, the fasting Respiratory Quotient (an index of nutrient utilization) is usually low (i.e., high fat utilization) in individuals who are metabolically healthy overweight/obese (e.g. MHO) than those who are metabolically unhealthy (e.g. MOOW) [31]. They also showed positive association between Respiratory Quotient and HOMA-IR; Therefore, in metabolically healthy individuals, IR tends to be low.

Moreover, our study revealed that frequency of IR was significantly high (63.2%) at younger (20–39 years) age group. This finding is in agreement with a recent Chinese study [32] that explored the aging-related changes of insulin secretion and insulin sensitivity among normal glucose tolerant (NGT) individuals. They found HOMA-IR negatively correlated with age among men and women even after adjusted for BMI and waist circumference in both univariate & multivariate linear regression and concluded that the basal postchallenge insulin secretion and postchallenge islet compensatory function decreases with aging, while insulin sensitivity does not deteriorate with aging and its related change of body composition and weight gain [32].

Furthermore, insulin resistance in young adults is often accompanied by a dyslipidemic profile [33,34]. Prevailing theories for the pathogenesis of insulin resistance focus on lipid-mediated mechanisms [35]; however, the etiology also involves obesity-induced metabolic by-products and inflammatory signaling [36].

On the contrary to our finding, a study found that insulin resistance and impaired glucose tolerance are commonly observed phenomena among elderly adults [37]. Aging is associated with detrimental changes in body composition, which persists even when elderly adults are matched to younger adults for BMI [38]. Adiposity, in particular abdominal adiposity, is well accepted determinant of insulin resistance and therefore may be a key mediator for the development of age-related insulin resistance. Despite an inverse relationship between age and insulin sensitivity [38,39], it remains contentious whether chronological age is a primary determinant of insulin resistance or age-related elevations in adiposity and/or physical inactivity are the primary causes of age-related insulin resistance [39,40]. So, there is a debate whether IR is higher in younger age or in older age which is yet to be resolved.

Our study also revealed that among the obesity phenotypes, females (67.5%) were more insulin resistant than males (48.1%). We also compared the gender-based frequency of insulin resistance in each obesity phenotypes. Frequency of insulin resistance found more in female than male in all obesity phenotypes except in MUO phenotype where males found to be more insulin resistant than females. This finding is in agreement with the finding of a cross sectional study on healthy young adults (mean age 19.2 years) that found IR more in female (15.9%) than male (9.1%) [41].

A recent study showed that adiposity indices including BMI, waist circumstance (WC), waist height ratio (WHtR) and waist hip ratio (WHR) are associated with IR [42]. Moreover, a systematic review and meta-analysis of observational studies showed a positive correlation between insulin resistance and obesity indices (BMI, WC, WHR) [43]. Waist circumference is linearly related to insulin resistance, and waist circumference, 85 cm is an optimal cutoff in predicting insulin resistance in middle-aged Japanese men [44].

Obesity, especially central obesity, has been demonstrated to be a risk factor for developing insulin resistance. One mechanism is that the excess visceral adipose tissue releases large amount of free fatty acids, which significantly impairs the insulin-signaling pathways in the main target organs [45]. Another mechanism is that inflammatory events inherent to obesity decrease the sensitivity to insulin in obese patients [45,46].

In our study, we used NCEP-ATP III criteria of metabolic syndrome for identifying obesity phenotypes in both sex. One of the components of these criteria is waist circumference. According to NCEP-ATP III criteria, men and women are centrally obese when waist circumference $\geq$102 cm and $\geq$88 cm respectively. Mean $\pm$ SD of WC for men and women were 96.5 ± 10.3 & 98.2 ± 7.6 respectively in our study. So, according to NCEP-ATP III criteria of metabolic syndrome, females of our study were more centrally obese than males. As central obesity has been demonstrated to be a risk factor for developing IR [45–47] and there is a positive correlation between WC and insulin resistance; so probably for this reason, we found more insulin resistance in our female subjects.

Nevertheless, according to a Spanish study; compared to women, men generally have more visceral adipose tissue (VAT) and less subcutaneous adipose tissue (SAT) [48]. Another study reported that greater amounts of visceral and hepatic adipose tissue, in conjunction with the lack of a possible protective effect of estrogen & lower adiponectin (insulin sensitizing hormone) levels, may be related to higher insulin resistance in men compared to women [49]. So, there is a debate in this area which needs to be explored in future.

5. Conclusion

Frequency of insulin resistance is alarmingly high (60.2%) in nondiabetic adult obese individuals. Among different obesity phenotypes, highest frequency of insulin resistance (76.3%) found in MUO phenotype and lowest frequency of IR (37.1%) found in MONW phenotype. Frequency of IR in MOOW and MHO phenotypes found 54.1 and 53.8% respectively.

Conflicts of interest

None of the authors have any conflict of interest to declare.

Acknowledgements

We are grateful to the volunteers for their participation and to all the employees of the outpatient department, BSMMU for their support during sample collection. This study was partly supported by internal grant of the Department of Biochemistry and Molecular Biology, BSMMU.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.dsx.2018.08.022.

References

[1] Haslam DW, James WP. Obesity. Lancet 2005;366:1197–209.
[2] Bray GA. Medical consequences of obesity. J Clin Endocrinol Metab 2004;89:2583–9.
[3] Roth J, Qiang X, Marban SL, Redelt H, Lowell BC. The obesity pandemic: where have we been and where are we going? Obes Res 2004;12:88S–101S.
[4] Jonathan CK. Commentary: the paradox of body mass index in obesity assessment: not a good index of adiposity, but not a bad index of cardiometabolic risk. Int J Epidemiol 2014;43:672–4.
[5] Mathew H, Farr OM, Mantzoros CS. Metabolic health and weight: understanding metabolically unhealthy normal weight or metabolically healthy obese patients. Metabolism 2016;65:73–80.
[6] Shea JL, King MT, Yi Y, Gulliver W, Sun G. Body fat percentage is associated with cardiometabolic dysregulation in BMI defined normal weight subjects. NutrMetabCardiovasc Dis 2012;22:741–7.
[7] Hamdy O, Porramatikul S, Al-Ozairi E. Metabolic obesity: the paradox between visceral and subcutaneous fat. Curr Diabetes Rev 2006;2:367–73.
[8] Pajunen P, Kotronen A, Korpi-Hyovalti E, Keinanen-Kiukaanniemi S, Oksa H, Niskanen L, et al. Metabolically healthy and unhealthy obesity phenotypes in the general population: the FIN-D2D Survey. BMC Publ Health 2011;11:1–8.
[9] Goday A, Calvo E, Vazquez LA, Caveda E, Margallo T, Catalina-Romero C, et al. Prevalence and clinical characteristics of metabolically healthy obese individuals and other obese/non-obese metabolic phenotypes in a working population: results from the Icaria study. BMC Publ Health 2016;16:1–14.
[10] World Health Organization. Obesity: preventing and managing the global epidemic, 252. Geneva, Switzerland: Report of a WHO consultation; 2000. Report No.: 894.
[11] Lee SH, Yang HK, Ha HS, Lee JH, Kwon HS, Park YM, et al. Changes in metabolic health status over time and risk of developing type 2 diabetes: a prospective cohort study. Medicine 2015;94. e1705.
[12] Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature 2006;444:840–6.
[13] Teixeira TF, Alves RD, Moreira AP, Peluzio Md. Main characteristics of metabolically obese normal weight and metabolically healthy obese phenotypes. Nutr Rev 2015;73:175–90.
[14] Kumar V, Abbas AK, Aster JC. In: Robbins basic pathology. ninth ed. Philadelphia: Elsevier Saunders; 2015. p. 742.
[15] Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412–9.
[16] Haffner SM, Kennedy E, Gonzalez C, Stern MP, Miettinen H. A prospective analysis of the HOMA model. The Mexico City Diabetes Study. Diabetes Care 1996;19:1138–41.
[17] Gonzalez-Ortiz M, Martinez-Abundis E. Comparison of several formulas to assess insulin action in the fasting state with the hyperglycemic-hyperinsulinemic clamp technique in healthy individuals. Rev Invest Clin 2003;55:419–22.
[18] Simental-Mendia LE, Rodriguez-Moran M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metab Syndrome Relat Disord 2008;6:299–304.
[19] Guerrero-Romero F, Villalobos-Molina R, Jimenez-Flores JR, Simental-Mendia LE, Mendez-Cruz R, Murguia-Romero M, et al. Fasting triglycerides and glucose index as a diagnostic test for insulin resistance in young adults. Arch Med Res 2016;47:e382–7.
[20] DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol 1979;237:214–23.

[21] Grundy SM, Cleeman JI, Daniels SR. Diagnosis and management of the metabolic syndrome: an american heart association/national heart, lung, and blood Institute scientific statement. Circulation 2005;112:2735–52.
[22] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; american heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. Circulation 2009;120:1640–5.
[23] Wildman RP, Muntner P, Reynolds K, McGinn AP, Rajpathak S, Wylie-Rosett J, et al. The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: prevalence and correlates of 2 phenotypes among the US population (NHANES 1999-2004). Arch Intern Med 2008;168:1617–24.
[24] Du T, Yuan G, Zhang M, Zhou X, Sun X, Yu X. Clinical usefulness of lipid ratios, visceral adiposity indicators, and the triglycerides and glucose index as risk markers of insulin resistance. Cardiovasc Diabetol 2014;13:146–55.
[25] Er LK, Wu S, Chou HH, Hsu LA, Teng MS, Sun YC. Triglyceride glucose-body mass index is a simple and clinically useful surrogate marker for insulin resistance in nondiabetic individuals. PLoS One 2016;11:1–12.
[26] Deepa R, Shanthirani CS, Premalatha G, Sastry NG, Mohan V. Prevalence of insulin resistance syndrome in a selected south Indian population-the Chennai urban population study-7 [CUPS-7]. Indian J Med Res 2002;115:118–27.
[27] Chandalia M, Abate N, Garg A, Stray-Gundersen J, Grundy SM. Relationship between generalized and upper body obesity to insulin resistance in Asian Indian men. J Clin Endocrinol Metab 1999;84:2329–35.
[28] Abassi F, Brown BW, Lamendola C, McLaughlin T, Reaven GM. Relationship between obesity, insulin resistance, and coronary heart disease. J Am Coll Cardiol 2002;40:937–43.
[29] Aguilar-Salinas CA, Garcia EG, Robles L, Riano D, Ruiz-Gomez DG, Garcia-Ulloa AC, et al. High adiponectin concentrations are associated with the metabolically healthy obese phenotype. J Clin Endocrinol Metab 2008;93:4075–9.
[30] Badman MK, Flier JS. The adipocyte as an active participant in energy balance and metabolism. Gastroenterology 2007;132:2103–15.
[31] Pujia A, Gazzaruso C, Ferro Y, Mazza E, Maurotti S, Russo C, et al. Individuals with metabolically healthy overweight/obesity have higher fat utilization than metabolically unhealthy individuals. Nutrients 2016;8:1–11.
[32] Zhu H, Yang Z, Zhang Bo, Xiao J, Yang W. Ageing related changes of insulin secretion and insulin sensitivity among normal glucose tolerance individuals in China. Natl Med J China (Peking) 2012;92:1948–53.
[33] Raitakari OT, Porkka KV, Ronnemaa T. The role of insulin in clustering of serum lipids and blood pressure in children and adolescents. The Cardiovascular Risk in Young Finns Study. Diabetologia 1995;38:1042–50.
[34] Moran A, Jacobs DR, Steinberger J, Steffen LM, Pankow JS, Hong CP, et al. Changes in insulin resistance and cardiovascular risk during adolescence: establishment of differential risk in males and females. Circulation 2008;117:2361–8.
[35] Savage DB, Petersen KF, Shulman GI. Disordered lipid metabolism and the pathogenesis of insulin resistance. Physiol Rev 2007;87:507–20.
[36] Muoio DM, Newgard CB. Mechanisms of disease: molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. Nat Rev Mol Cell Biol 2008;9:193–205.
[37] Short KR, Bigelow ML, Kahl J, Singh R, Coenen-Schimke J, Raghavakaimal S, et al. Decline in skeletal muscle mitochondrial function with aging in humans. Proc Natl Acad Sci USA 2005;102:5618–23.
[38] Short KR, Vittone JL, Bigelow ML, Proctor DN, Rizza RA, Coenen-Schimke JM, et al. Impact of aerobic exercise training on age-related changes in insulin sensitivity and muscle oxidative capacity. Diabetes 2003;52:1888–96.
[39] Petersen KF, Dufour S, Befroy D, Garcia R, Shulman GI. Impaired mitochondrial activity in the insulin-resistant offspring of patients with type 2 diabetes. N Engl J Med 2004;350:664–71.
[40] Basu R, Breda E, Oberg AL, Powell CC, Dalla Man C, Basu A, et al. Mechanisms of the age-associated deterioration in glucose tolerance: contribution of alterations in insulin secretion, action, and clearance. Diabetes 2003;52:1738–48.
[41] Guerrero-Romero F, Villalobos-Molina R, Jimenez-Flores JR, Simental-Mendia LE, Mendez-Cruz R, Murguia-Romero M, et al. Fasting triglycerides and glucose index as a diagnostic test for insulin resistance in young adults. Arch Med Res 2016;47:e382–7.
[42] Pan SY, Groh M, Aziz A, Morrison H. Relation of insulin resistance with social-demographics, adiposity and behavioral factors in non-diabetic adult Canadians. J Diabetes Metab Disord 2016;15:1–11.
[43] Zhang M, Hu T, Zhang S, Zhou L. Associations of different adipose tissue depots with insulin resistance: a systematic review and meta-analysis of observational studies. Sci Rep 2015;5:1–6.
[44] Tabata S, Yoshimitsu S, Hamachi T, Abe H, Ohnaka K, Kono S. Waist circumference and insulin resistance: a cross-sectional study of Japanese men. BMC Endocr Disord 2009;9:1–7.
[45] Mercurio V, Carlomagno G, Fazio V, Fazio S. Insulin resistance: is it time for primary prevention? World J Cardiol 2012;4:1–7.
[46] Zeyda M, Stulnig TM. Obesity, inflammation, and insulin resistance-a mini review. Gerontology 2009;55:379–86.
[47] Kim SH, Abbasi F, Reaven GM. Impact of degree of obesity on surrogate estimates of insulin resistance. Diabetes Care 2004;27:1998–2002.
[48] Garaule M, Perex-Llamas F, Fuente T. Anthropometric, computed tomography and fat cell data in an obese population: relationship with insulin, leptin, tumor necrosis factor-alpha, sex hormone-binding globulin and sex hormones. Eur J Endocrinol 2000;143:657–66.
[49] Geer EB, Shen W. Gender differences in insulin resistance, body composition, and energy balance. Gend Med 2009;6:60–75.