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The informational value of percent body fat integrating with body mass index associated with risk of abnormal blood glucose

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ABSTRACT

Objective: The purpose of the study is to examine the value of percent body fat (%BF) with BMI to assess the risk of abnormal blood glucose (ABG) among US adults who are normal weight or overweight. We hypothesized that normal weight population with higher %BF is more likely to have ABG.

Design: A cross-sectional study.

Setting: National Health and Nutritional Examination Survey (NHANES), 1999–2006, conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention.

Participants: Participants were US adults aged 40 and older who have never been diagnosed with type 2 diabetes by a doctor (unweighted N=9790, weighted N=101098270). The study population was classified into four groups: 1) normal weight with normal %BF, 2) normal weight with high %BF, 3) overweight with normal %BF and 4) overweight with high %BF.

Main outcome measures: Odds ratios for abnormal blood glucose including prediabetes and undiagnosed diabetes (HbA1c>=5.7%).

Results: 64% were misclassified as normal despite high %BF. Prevalence of ABG in normal weight group with high %BF (13.5%) is significantly higher than overweight group with lower %BF (p<.00). In an unadjusted model, the odds ratio of ABG was significantly greater in adults at normal BMI with high %BF compared to individuals at normal weight with lower %BF. In an adjusted model controlling for age, sex, race/ethnicity, first degree of relative diabetes, vigorous-intensity activities and muscle strengthening activities, risks of ABG were greater in population with normal weight and high %BF and with overweight and low %BF(OR, 1.55, 95% CI, 1.01-2.38, p<.05 vs. OR, 1.17, 95% CI, 0.69-1.98).

Conclusions: Integrating BMI with %BF can improve in classification to direct screening and prevention efforts to a group currently considered healthy and avoid penalties and stigmatization of other groups that are misclassified as unhealthy.

Keywords: abnormal glucose, diabetes prevention, percent body fat, body mass index

Strengths and limitations of this study

- The study used population-based nationally representative data allowing for generalizability.
- We used the most accurate body composition measurement, DXA to assess direct impact of excessive body fat on abnormal blood glucose.
- Percent body fat integrating with BMI improved classification of population who has excessive body fat associated with high risk of abnormal blood glucose.
- The data is relatively old while it is the most recent data including whole body DXA measurement.
- There is no gold standard cut off points in defining obesity according to percent body fat.

Introduction

Diabetes has become a worldwide epidemic. It is one of leading causes of morbidity and mortality in the US and its prevalence has been steadily increasing (1, 2). The prevalence of diagnosed diabetes reached to 12.3% of US adults in 2011-2012. [1] Furthermore, the total direct medical costs for diabetes was $176 billion in 2012 and health care expenditure for people with diabetes is more than 2 times higher than people without diabetes (3).

In an effort to prevent diabetes and identify patients with undiagnosed diabetes for potential treatment, the United States Preventive Services Task Force (USPSTF) recommends screening asymptomatic adults for abnormal blood glucose (prediabetes or undiagnosed diabetes) (4, 5). The USPSTF recommends screening adults aged 40-70 only if they are overweight or obese using body mass index (BMI) cutoffs (USPSTF, 2014). Recently, the Equal Employment Opportunity Commission (EEOC) proposed the rule that if employees who are overweight or obese fail to achieve a normal weight (18.5-24.9kg/m^2) through wellness programs, they penalize the employees who participate into wellness program up to 30% of the total costs of health insurance (6). Consequently, BMI levels have substantial implications for defining someone as healthy or unhealthy.

BMI which is widely adopted to assess obesity-related risk in clinical setting, however, may misclassify some segments of the general population who are at metabolic risk. BMI is based on height and weight and body weight that includes not only body fat but also muscle, bone and body water (7). Recent studies found that half of people who were obese according to percent body fat (%BF) but were classified as normal weight defining by BMI, and about 18% of adults with excessive %BF who were misclassified as not obese showed a significant higher prevalence of metabolic syndrome (8, 9). Recent data indicates that a significant proportion of people with a normal weight designated by BMI (18.5-24.9 kg/m^2) have prediabetes, undiagnosed diabetes and hypertension (10-12). In fact, 33% of adults 45 and older at a normal weight have prediabetes. Moreover, normal weight obesity (NWO) which represents an individual who fall into normal range of BMI and who have excessive body fat mass is associated with higher risk of metabolic syndrome, cardiometabolic dysregulation and cardiovascular mortality (13, 16). On the other hand, professional football players who are

typically classified as being obese due to high muscle mass actually showed better cardiovascular health compared to the general population (17).

Because of the possible deleterious consequences due to BMI misclassification, percent body fat (%BF) may have some value as an addition to BMI to improve classification of individuals as healthy or unhealthy in terms of abnormal blood glucose (14, 15, 18). However, the extent to which adding %BF to BMI improves classification of risk is unclear. There has been little investigation to determine the incremental value of combining BMI and %BF in a risk assessment for abnormal blood glucose. Therefore, the purpose of this study is to examine in a nationally representative sample the value of %BF with BMI to assess the risk of abnormal glucose among adults who are normal weight or overweight and improve classification.

Methods

We analyzed the nationally representative, National Health and Nutrition Examination Survey (NHANES) for the years of 1999-2006. Although there are more recent NHANES data, this is the most recent data with a whole body Dual-energy X-ray Absorptiometry (DXA) which measures %BF. The NHANES is a national representative survey of noninstitutionalized US population using a complex stratified multistage probability cluster sample design. To account for nationally representative population estimates, the National Center for Health Statistics (NCHS) applies a multilevel weighting system. The survey included a standardized medical examination including blood and urine analysis for examining biomarkers and a number of health-related interviews. The current study was approved as exempt by the Institutional Review Board (IRB) at the University of Florida.

Anthropometric Assessment

BMI was obtained from body weight divided by height squared (kg/m^2). Weight and height were measured by a trained examiner in the mobile examination center and these were used to calculate BMI (19). BMI values were categorized into four groups (i.e., underweight, normal weight, overweight and obesity) on the basis of WHO guideline (7). Percent body fat (%BF) was derived from 1-3 times weekly measured whole body DXA scan (Hologic, Inc., Bedford, Massachusetts) (20). A sex-specific threshold of %BF was adopted as 25% for men and 32% for women from preliminary studies (14, 15, 18).

Participants

The current study focused on adults aged over 40 or older who have never been told by a doctor or a health professional that they have diabetes (unweighted n=9,790). We focused on individuals 40 and older since 40 is the lower age cutoff for screening for abnormal blood glucose as suggested by the USPSTF. [4] The study population was individuals with normal weight or overweight as defined by BMI. We limited the study to these individuals because they were the groups most likely to potentially be reclassified by the addition of %BF to BMI.

Participants were classified into four groups based on combined BMI and %BF. In normal BMI (18.5-24.9 kg/m^2), the first group would be assessed to be at low risk based on being normal on two different criteria (normal BMI and low %BF). The second group may be misclassified as healthy even though existing data suggests a substantial population have prediabetes (normal BMI but high %BF) (12). Among individuals classified as overweight by BMI (25-29.9 kg/m^2), the third group may be misclassified as unhealthy, but they may be healthy due to the BMI limitation of not appropriately assessing extensive muscle mass (overweight and low %BF). The fourth group would be at high risk based on having excessive fat (overweight and high %BF). Pregnant women who were not allowed to test the DXA examination were excluded. Also we excluded the obese population because of the known high risk.

Outcomes

The primary outcome is an abnormal glucose including prediabetes or undiagnosed diabetes, an HbA1c level of 5.7% or higher. All subjects reported never having been told by a doctor or a health professional that they had prediabetes or diabetes (5). We excluded individuals with an HbA1c of 4.0% (20 mmol/mol) that is associated with increased mortality without diabetes (21).

Covariates

Age was classified into two groups with cut offs of 40 and 71 years old. Race/ethnicity was categorized into four groups, 1) Non-Hispanic White, 2) Non-Hispanic Black, 3) Hispanics and 4) Other. Family history of diabetes was defined as a report of a first degree of relative ever being told by a health professional that they had diabetes.

Although, not specifically seen as a potential confounder we also assessed physical activity. Vigorous activity was defined as reports of an activity that causes light seating or a slight to moderate increase in breathing or heart rate for at least 10 minutes over the past 30 days. Muscle strengthening activity refers to any physical activities designed to strengthen muscles including lifting weights, push-ups or sit-ups over the past 30 days.

Statistical Analysis

To account for the stratified multistage probability sample design, we used SAS 9.4 (Cary, NC) and SUDAAN software (RTI, NC) for data analyses. Weighting and design variables applied to all analyses from univariate analyses, chi-square tests and logistic regression models. They allow us to estimate population estimates for noninstitutionalized US population. We examined bivariate relationship between combined BMI/%BF and abnormal glucose. Following by, both unadjusted and adjusted logistic regressions controlling for age, sex, race/ethnicity, family history of diabetes, vigorous activity and muscle strengthening activity was employed to assess likelihood of having abnormal blood glucose.

Results

The total unweighted sample size was 9,790 adults representing 101,098,270 adults in the US population. Table 1 showed that among normal weight population, approximately 64% were misclassified as normal despite high %BF. Prevalence of abnormal glucose by combined BMI and %BF is shown in Table 2. Prevalence of abnormal glucose in normal weight group with high %BF (13.5%) is significantly higher than overweight group with lower %BF (10.5%) ($p<.00$). About 78% of population was adults aged between 40 to 70 and non-Hispanic White. In sex, most men showed low %BF whereas more than 70% of women has excessive body fat within normal weight population. Regardless of BMI, more than 40% of population with low %BF performed vigorous-intensity activity as well as muscle strengthening activity compared to population with high %BF ($p<.00$).

In an unadjusted logistic regression, the odds ratio of abnormal glucose was significantly greater in adults at normal weight with high %BF compared to individuals at normal weight with low %BF as the reference group (Table 3). Conversely, abnormal glucose risk was not significantly more likely in overweight adults with low %BF when compared to the normal weight/low %BF group. In an adjusted model controlling for age, sex, race/ethnicity, first degree of relative diabetes, vigorous-intensity activities and muscle strengthening activities the adjusted model results were similar to the unadjusted results. Risks of abnormal glucose were greater in population with normal weight and high %BF and with overweight and low %BF, whereas only odds ratios among individuals with high %BF were significantly higher compared with the reference group (Table 3).

Discussion

The use of BMI only may misclassify segments of the adult population in terms of abnormal glucose. Our key findings showed that individuals with normal weight who have excessive percent body fat (%BF) have significantly higher risk of abnormal glucose compared with individuals with normal weight and low %BF. Conversely, of individuals with overweight, low %BF is not significantly associated with the risk of abnormal glucose. The results suggest that %BF combined with BMI may help to improve risk stratification for abnormal blood glucose in these intermediate groups.

Since body weight comprises not only fat but also a variety of body compositions such as muscle, organs and body water, it may not estimate actual amount of body fat. Professional football players who are typically classified as obesity due to high muscle mass showed better cardiovascular health compared to general population (17). In addition, among military population, whereas an average of BMI was overweight, almost half of them had never had any form of sickness absence (22). These evidences indicate that %BF may be a key factor in estimating risk of chronic disease and it may provide more valuable evidence of obesity-induced inflammatory pathway beyond simply measuring BMI.

Our key findings may suggest refinement of current clinical guidelines with additional body composition assessments. The USPSTF and the American Diabetes Association (ADA) have BMI as a key component of recommendations for diabetes prevention (4, 5). There may be missed opportunities for screening, particularly for prediabetes. Using a concept of normal weight obesity has an opportunity to better detect this at risk population to receive appropriate prevention services. It is also important, as shown in our findings, that we appropriately classify the overweight population with low %BF. This population has been neglected as being classified as a healthy population. These individuals are more likely to perform high-intensity physical activities. Professional athletes or civil forces with higher muscle mass who are typically classified as obesity measured by BMI may fail to meet normal BMI criteria in recruitment screening (23). In addition, according to the rule offered by EEOC, employees who are classified as overweight or obesity with high muscle mass and lower body fat may get penalized (6). To prevent these adverse events, more accurate body composition assessment may be required.

Limitations

There are limitations to this study. First, there is no gold standard clinical cut point to indicate high or low percentage body fat. While numerous studies used a variety of sex-specific thresholds, sensitivity analysis has not been implemented yet. The current study however, adopted commonly used criteria as a way to promote generalizability and comparability to other studies. Second, although this is a study investigating the association between several physiological measures, the data is not the most recent NHANES and so population estimates may not totally represent the current US population. While there are more recent NHANES data, the data used in the study is the most recent data with a whole body DXA measurement. We felt that the validity of the DXA scan for %BF was a strength that outweighed the recent data collection. Third, our analyses were cross sectional and did not allow us to look at the downstream risks of individuals with normal weight obesity. However, our primary goal was to improve on BMI in the accuracy of screening guidelines for individuals with current abnormal blood glucose which thereby requires cross-sectional analyses.

Conclusion

BMI which is typically used to define normal weight or overweight in a clinical setting may misclassify populations in relation to abnormal blood glucose. Integrating BMI with %BF can help in classification to direct screening and prevention efforts to a group currently considered healthy and avoid penalties and stigmatization of other groups that are misclassified as unhealthy.

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Contributors:

Ara Jo, MS led the entire research as the first author from writing the manuscript, analyzing the data and interpretation.

Dr. Arch G. Mainous, PhD supervised the entire process of the research as a research mentor and contributed to writing the manuscript.

Competing interests: None declared.

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Ethics approval: This study was approved as exempt by the Institutional Review Board at the University of Florida.

Data sharing statement: Data are available through the National Health and Nutrition Examination Survey access from https://www.cdc.gov/nchs/nhanes/index.htm.

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Table 1. BMI Misclassification among US Adults aged over 40 or older who are Normal weight and Overweight Stratified by BMI and %BF (Unweighted N=9,790 and Weighted N=101,098,270)

Group	BMI (kg/m^2)	%BF	Proportion (%)
1	Normal (18.5-24.9 kg/m^2)	Low	36.3
2		High	63.7
3	Overweight (25.0-29.9 kg/m^2)	Low	9.0
4		High	91.0

Table 2. Baseline characteristics of adults aged over 40 or older who are normal weight and overweight (Unweighted N=9,790 and Weighted N=101,098,270)

Body Mass Index	Normal		Overweight		p-value
% of Body Fat	Low	High	Low	High	
Weighted Sample size	812522	2248425	312588	6105346	
Prevalence of Abnormal Glucose	8.6	13.5	10.5	20.0	<.00
Age					
40 to 70	92.3	81.1	96.0	85.2	<.00
71 or older	7.7	18.9	4.0	14.8	
Sex					
Men	61.1	28.8	96.2	53.4	<.00
Women	38.9	71.2	3.8	46.6	
Race					
Non-Hispanic White	77.7	80.4	70.4	77.0	<.00
Non-Hispanic Black	8.2	4.8	17.0	8.0	
Hispanics	9.1	7.1	10.0	10.9	
Others	4.3	7.7	2.6	4.2	
First Degree Relative Diabetes					
Yes	35.9	45.5	43.6	46.9	<.00
No	64.2	54.5	56.4	53.1	
Vigorous Activity					
Yes	41.7	28.1	45.9	30.4	<.00
No	58.3	71.9	54.1	69.6	
Muscle Strengthening Activities					
Yes	40.5	25.1	38.1	23.4	<.00
No	59.5	74.9	61.9	76.7	

Table 3. Odds Ratios (95% Confidence Intervals) for the Abnormal Glucose for Adults with Normal Weight and Overweight in Unadjusted and Adjusted Models controlling for age, sex, race/ethnicity, first degree relative diabetes, vigorous activities, and muscle strengthening activity

BMI	%BF	Unadjusted OR	Adjusted OR
Normal (18.5-24.9kg/m^2)	Low	1.00	1.00
	High	1.66 (1.13-2.43)*	1.55 (1.01-2.38)*
Overweight (25-29.9kg/m^2)	Low	1.25 (0.75-2.07)	1.17 (0.69-1.98)
	High	2.64 (1.86-3.76)*	2.45 (1.61-3.71)*

*** statistically significant at .05**

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 15
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	7, 16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8,9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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ABSTRACT

Objective: To examine the value of percent body fat (%BF) with BMI to assess the risk of abnormal blood glucose (ABG) among US adults who are normal weight or overweight. We hypothesized that normal weight population with higher %BF is more likely to have ABG.

Design: A cross-sectional study.

Setting: National Health and Nutritional Examination Survey (NHANES), 1999–2006, conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention.

Participants: Participants were US adults aged 40 and older who have never been diagnosed with type 2 diabetes by a doctor (unweighted N=6335, weighted N=65705694). The study population was classified into four groups: 1) normal weight with normal %BF, 2) normal weight with high %BF, 3) overweight with normal %BF and 4) overweight with high %BF.

Main outcome measures: Odds ratios for ABG including prediabetes and undiagnosed diabetes (HbA1c≥5.7%, ≥39 mmol/mol).

Results: 64% of normal weight population with high %BF were misclassified as normal. Prevalence of ABG in normal weight group with high %BF (13.5%) is significantly higher than the overweight group with lower %BF (p<.001). In an unadjusted model, the odds ratio of ABG was significantly greater in adults at normal BMI with high %BF compared to individuals at normal weight with lower %BF. In an adjusted model controlling for age, sex, race/ethnicity, first degree of relative diabetes, vigorous-intensity activities and muscle strengthening activities, risks of ABG were greater in population with normal weight and high %BF and with overweight and low %BF(OR, 1.55, 95% CI, 1.01-2.38, p<.05 vs. OR, 1.17, 95% CI, 0.69-1.98).

Conclusions: Integrating BMI with %BF can improve in classification to direct screening and prevention efforts to a group currently considered healthy and avoid penalties and stigmatization of other groups that are misclassified as unhealthy.

Keywords: abnormal glucose, diabetes prevention, percent body fat, body mass index

Strengths and limitations of this study

- The study used population-based nationally representative data allowing for generalizability.
- We used the most accurate body composition measurement, DXA to assess direct impact of excessive body fat on abnormal blood glucose.
- Percent body fat integrating with BMI improved classification of population who has excessive body fat associated with high risk of abnormal blood glucose.
- The data is relatively old while it is the most recent data including whole body DXA measurement.
- There is no gold standard cut off points in defining obesity according to percent body fat.

Introduction

Diabetes has become a worldwide epidemic. It is one of leading causes of morbidity and mortality in the US and its prevalence has been steadily increasing (1, 2). The prevalence of diagnosed diabetes reached to 12.3% of US adults in 2011-2012 (1). Furthermore, the total direct medical costs for diabetes was $176 billion in 2012 and health care expenditure for people with diabetes is more than 2 times higher than people without diabetes (3).

In an effort to prevent diabetes and identify patients with undiagnosed diabetes for potential treatment, the United States Preventive Services Task Force (USPSTF) recommends screening of abnormal blood glucose (prediabetes or undiagnosed diabetes) for asymptomatic adults (4, 5). The USPSTF recommends screening adults aged between 40years old and 70 years old only if they are overweight or obese defined by body mass index (BMI) cutoffs (4). Recently, the Equal Employment Opportunity Commission (EEOC) proposed the rule that if employees who are overweight or obese fail to achieve a normal weight (18.5-24.9kg/m^2) through wellness programs, they penalize the employees who participate into wellness program up to 30% of the total costs of health insurance (6). Consequently, BMI levels have substantial implications for defining someone as healthy or unhealthy.

BMI which is widely adopted to assess obesity-related risk in clinical setting, however, may misclassify some segments of the general population who are at metabolic risk. While BMI is a simple equation based on height and weight, body weight that includes not only body fat but also muscle, bone and body water (7). Recent studies found that half of people who were obese according to percent body fat (%BF) but were classified as normal weight defined by BMI, and about 18% of adults with excessive %BF who were misclassified as not being obese showed a significant higher prevalence of metabolic syndrome (8, 9). Recent data indicates that a significant proportion of people with a normal weight designated by BMI (18.5-24.9 kg/m^2) have prediabetes, undiagnosed diabetes and hypertension (10-12). In fact, 33% of adults 45 years old and older at a normal weight have prediabetes. Moreover, a normal weight obesity (NWO) which represents an individual who fall into normal range of BMI and who have excessive body fat mass is associated with higher risk of metabolic syndrome, cardiometabolic dysregulation and cardiovascular mortality (13, 16). On the other hand, professional football players who are

typically classified as being obese due to high muscle mass actually showed better cardiovascular health compared to the general population (17).

Because of the possible deleterious consequences due to BMI misclassification, percent body fat (%BF) may have some value as an addition to BMI to improve classification of individuals as healthy or unhealthy in terms of abnormal blood glucose (14, 15, 18). However, the extent to which adding %BF to BMI improves classification of risk is unclear. There has been little investigation to determine the incremental value of combining BMI and %BF in a risk assessment for abnormal blood glucose. Therefore, the purpose of this study is to examine in a nationally representative sample the value of %BF with BMI to assess the risk of abnormal glucose among adults who are normal weight or overweight and improve classification.

Methods

We analyzed the nationally representative, National Health and Nutrition Examination Survey (NHANES) for the years of 1999-2006. Although there are more recent NHANES data, this is the most recent data with a whole body Dual-energy X-ray Absorptiometry (DXA) which measures %BF. The NHANES is a national representative survey of noninstitutionalized US population using a complex stratified multistage probability cluster sample design. To account for nationally representative population estimates, the National Center for Health Statistics (NCHS) applies a multilevel weighting system. The survey included a standardized medical examination including blood and urine analysis for examining biomarkers and a number of health-related interviews. The current study was approved as exempt by the Institutional Review Board (IRB) at the University of Florida.

Anthropometric Assessment

BMI was obtained from body weight divided by height squared (kg/m^2). Weight and height were measured by a trained examiner in the mobile examination center and these were used to calculate BMI (19). BMI values were categorized into four groups (i.e., underweight, normal weight, overweight and obesity) on the basis of WHO guideline (7). Percent body fat (%BF) was derived from 1-3 times weekly measured whole body DXA scan (Hologic, Inc., Bedford, Massachusetts) (20). A sex-specific threshold of %BF was adopted as 25% for men and 35% for women given by the WHO guideline (Obesity in men ≥25% and women ≥35%) (7).

Participants

The current study focused on adults aged over 40 years old or older who have never been told by a doctor or a health professional that they have diabetes (unweighted n=6,335). We focused on individuals 40 years old and older since 40 years old is the lower age cutoff for screening for abnormal blood glucose as suggested by the USPSTF(4). The study population was individuals with normal weight or overweight as defined by BMI. We limited the study to these individuals because they were the groups most likely to potentially be reclassified by the addition of %BF to BMI.

Participants were limited to normal weight and overweight population (18.5-29.9 kg/m^2) and classified into four groups based on combined BMI and %BF. Respondents who were underweight and obesity defined by BMI were excluded (missing N=5,744). In normal BMI (18.5-24.9 kg/m^2), the first group who had normal BMI and low %BF would be assessed to be at low risk. The second group may be misclassified as healthy even though existing data suggests a substantial population have prediabetes (normal BMI but high %BF) (12). Among individuals classified as overweight by BMI (25-29.9 kg/m^2), the third group may be misclassified as unhealthy, but they may be healthy due to the BMI limitation of not appropriately assessing extensive muscle mass (overweight and low %BF). The fourth group would be at high risk based on having excessive fat (overweight and high %BF). Pregnant women who were not allowed to test the DXA examination were excluded. Also we excluded the obese population because of the known high risk.

Outcomes

The primary outcome is an abnormal glucose including prediabetes or undiagnosed diabetes, an HbA1c level of 5.7% or higher (≥39mmol/mol). All subjects reported never having been told by a doctor or a health professional that they had prediabetes or diabetes (5). We excluded individuals with an HbA1c of 4.0% (≤20 mmol/mol) that is associated with increased mortality without diabetes (21).

Covariates

Age was classified into two groups with cut offs of 40 years old and 71 years old. Race/ethnicity was categorized into four groups, 1) Non-Hispanic White, 2) Non-Hispanic Black, 3) Hispanics and 4) Other. Family history is a predictor of diabetes according to preliminary study (22). Thus we selected family history of diabetes representing a first degree of relative ever being told by a health professional that they had diabetes.

We also assessed physical activity. Intense activity helps to increase muscle mass and reduce body fat and it may result in overweight despite low %BF. Also physical activity represents a lifestyle intervention to control blood glucose. Vigorous activity was defined as reports of an activity that causes a slight to moderate increase in breathing or heart rate for at least 10 minutes over the past 30 days. Muscle strengthening activity refers to any physical activities designed to strengthen muscles including lifting weights, push-ups or sit-ups over the past 30 days.

Statistical Analysis

To account for the stratified multistage probability sample design, we used SAS 9.4 (Cary, NC) and SUDAAN software (RTI, NC) for data analyses. Weighting and design variables applied to all analyses from univariate analyses, chi-square tests and logistic regression models. They allow us to estimate population estimates for noninstitutionalized US population. We examined bivariate relationship between combined BMI/%BF and abnormal glucose. Following by, both unadjusted and adjusted logistic regressions controlling for age, sex, race/ethnicity, family history of diabetes, vigorous activity and muscle strengthening activity was employed to assess likelihood of having abnormal blood glucose.

Results

The total unweighted sample size was 6,335 US adults representing 65,705,694 adults in the US population. No variable had more than 3% unweighted missing data and none of the demographics had any missing data. It is important to note that the population estimates are based on weighted sample. Table 1 showed that among normal weight population, approximately 64% of the normal weight population were misclassified as normal despite a high level of %BF. Prevalence of abnormal glucose by combined BMI and %BF is shown in Table 2. Prevalence of abnormal blood glucose in the normal weight group with high %BF (13.5%) is significantly higher than the overweight group with lower %BF (10.5%) (p<.001). About 78% of the study population was adults aged between 40 years old to 70 years old and Non-Hispanic White. In sex, most men showed low %BF whereas more than 70% of women has a high level of a body fat within normal weight population. Regardless of BMI, more than 40% of the study population with low %BF performed vigorous-intensity activity as well as muscle strengthening activity compared to population with high %BF (p<.001).

In an unadjusted logistic regression, the odds ratio of abnormal glucose was significantly greater in adults at normal weight with high %BF compared to individuals at normal weight with low %BF as the reference group (Table 3). Conversely, abnormal blood glucose risk was not significantly more likely in overweight adults with low %BF when compared to the normal weight/low %BF group. In an adjusted model controlling for age, sex, race/ethnicity, first degree of relative diabetes, vigorous-intensity activities and muscle strengthening activities, the adjusted model results were similar to the unadjusted results. Risks of abnormal blood glucose were greater in population with normal weight and high %BF as well as the overweight with high %BF (Table 3).

In sensitivity analyses, Area Under the Curve (AUC) of combined form of BMI and %BF was larger than areas of BMI only or %BF only (Figure 1). These areas were significantly different (p<.001).

Discussion

The use of BMI only may misclassify segments of the adult population in terms of abnormal glucose. Our key findings showed that individuals with normal weight who have excessive percent body fat (%BF) have significantly higher risk of abnormal glucose compared with individuals with normal weight and low %BF. Conversely, of individuals with overweight, low %BF is not significantly associated with the risk of abnormal glucose. The results suggest that %BF combined with BMI may help to improve risk stratification for abnormal blood glucose in these intermediate groups.

Since body weight comprises not only fat but also a variety of body compositions such as muscle, organs and body water, it may not estimate actual amount of body fat. Professional football players who are typically classified as obesity due to high muscle mass showed better cardiovascular health compared to general population (17). In addition, among military population, whereas an average of BMI was overweight, almost half of them had never had any form of sickness absence (23). Furthermore, since according to our preliminary study, 33% of normal weight population has prediabetes, %BF may identify this normal weight population at risk of development of ABG (11). These evidences indicate that %BF may be a key factor in improving to estimate risk of chronic disease.

Our key findings may suggest refinement of current clinical guidelines with additional body composition assessments. The USPSTF and the American Diabetes Association (ADA) have BMI as a key component of recommendations for diabetes prevention (4, 5). There may be missed opportunities for screening, particularly for prediabetes. Regardless of BMI, people with high %BF were older, female and Non-Hispanic White. While the proportion of family history patients with a positive for diabetes was similar across four groups, physical activity was different among groups. It is particularly important, as shown in our findings, that we appropriately classify the overweight population with low %BF. This population has been neglected as being classified as a healthy population. Our finding showed that these individuals are significantly more likely to perform high-intensity physical activities compared to the normal weight population who had low %BF and this behavior may result in overweight. For instance, professional athletes or civil forces with higher muscle mass who are typically classified as obesity measured by BMI may fail to meet normal BMI criteria in recruitment screening (24). In addition, according to the rule offered by EEOC, employees who are classified as overweight or obesity with high muscle mass and lower body fat may get penalized (6). Our findings indicated that BMI may not be the optimal tool to assess health outcomes for employees and new rule of the EEOC should be modified to consider body fat instead of body weight. Using a concept of normal weight obesity has also an opportunity to better detect population at risk of abnormal blood glucose to receive appropriate prevention services. This strategy may detect more than 303,000 US adults who are normal weight and who usually miss an opportunity to receive preventive care service on time due to the use of BMI only. To prevent these adverse events, more accurate body composition assessment may be required.

A direction for future research might be to refine the cut points for %BF, particularly in a longitudinal cohort. Further, it may be important to consider some other variables that may confound the relationship between %BF and diabetes like poverty, smoking, and sleep (25, 26).

Limitations

There are limitations to this study. First, there is no gold standard clinical cut point to indicate high or low percentage body fat. While numerous studies used a variety of sex-specific thresholds, sensitivity analysis has not been implemented yet. The current study however, adopted commonly used criteria as a way to promote generalizability and comparability to other studies. Second, although this is a study investigating the association between several physiological measures, the data is not the most recent NHANES and so population estimates may not totally represent the current US population. While there are more recent NHANES data, the data used in the study is the most recent data with a whole body DXA measurement. We felt that the validity of the DXA scan for %BF was a strength that outweighed the recent data collection. Third, our analyses were cross sectional and did not allow us to look at the downstream risks of individuals with normal weight obesity. However, our primary goal was to improve on BMI in the accuracy of screening guidelines for individuals with current abnormal blood glucose which thereby requires cross-sectional analyses. Lastly, the use of a DXA scan may be an economic burden in health care setting. While a DXA scan is the most accurate technique to measure body compositions, it is prohibitively expensive to use for the purpose of screening only. Current insurance company does not cover the use of DXA scan for the purpose of screening of chronic diseases. Bioelectrical Impedance Analysis (BIA) which assesses %BF may be a cost-effectiveness alternative for the purpose of ABG screening in primary care setting, while current study used the data measured by DXA scan.

Conclusion

BMI which is typically used to define normal weight or overweight in a clinical setting may misclassify populations in relation to abnormal blood glucose. Integrating BMI with %BF can help in classification to direct screening and prevention efforts to a group currently considered healthy and avoid penalties and stigmatization of other groups that are misclassified as unhealthy.

Acknowledgments

Contributors:

Ara Jo, PhD led the entire research as the first author from writing the manuscript, analyzing the data and interpretation.

Dr. Arch G. Mainous III, PhD supervised the entire process of the research as a research mentor and contributed to writing the manuscript.

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Ethics approval: This study was approved as exempt by the Institutional Review Board at the University of Florida.

Data sharing statement: Data are available through the National Health and Nutrition Examination Survey access from https://www.cdc.gov/nchs/nhanes/index.htm.

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Table 1. BMI Misclassification among US Adults aged over 40 or older who are Normal weight and Overweight Stratified by BMI and %BF (Unweighted N=6,335 and Weighted N=65,705,694)

		BMI (kg/m^2)	
		Normal (18.5-24.9 kg/m^2)	Overweight (25.0-29.9 kg/m^2)
%BF	Low	36.3	9.0
	High	63.7	91.0

Table 2. Baseline characteristics of adults aged over 40 or older who are normal weight and overweight (Unweighted N=6,335 and Weighted N= 65,705,694)

Body Mass Index	Normal		Overweight		p-value
% of Body Fat	Low	High	Low	High	
Unweighted Sample Size	908	1679	327	3421	
Weighted Sample Size	10259138	18020486	3382474	34043596	
Prevalence of Abnormal Blood Glucose	8.6	13.5	10.5	20.0	<.001
Age					
40 to 70	92.3	81.1	96.0	85.2	<.001
71 or older	7.7	18.9	4.0	14.8	
Sex					
Men	61.1	28.8	96.2	53.4	<.001
Women	38.9	71.2	3.8	46.6	
Race					
Non-Hispanic White	77.5	80.4	70.4	77.0	<.001
Non-Hispanic Black	11.7	4.8	17.0	8.0	
Hispanics	6.5	7.1	10.0	10.9	
Others	4.3	7.7	2.6	4.2	
First Degree Relative Diabetes					
Yes	35.9	45.5	43.6	46.9	<.001
No	64.2	54.5	56.4	53.1	
Vigorous Activity					
Yes	41.7	28.1	45.9	30.4	<.001
No	58.3	71.9	54.1	69.6	
Muscle Strengthening Activities					
Yes	40.5	25.1	38.1	23.4	<.001
No	59.5	74.9	61.9	76.7	

Table 3. Odds Ratios (95% Confidence Intervals) for the Abnormal Glucose for Adults with Normal Weight and Overweight in Unadjusted and Adjusted Models controlling for age, sex, race/ethnicity, first degree relative diabetes, vigorous activities, and muscle strengthening activity

BMI	%BF	Unadjusted OR	Adjusted OR
Normal (18.5-24.9kg/m^2)	Low	1.00	1.00
	High	1.66 (1.13-2.43)*	1.55 (1.01-2.38)*
Overweight (25-29.9kg/m^2)	Low	1.25 (0.75-2.07)	1.17 (0.69-1.98)
	High	2.64 (1.86-3.76)*	2.45 (1.61-3.71)*

*** statistically significant at .05**

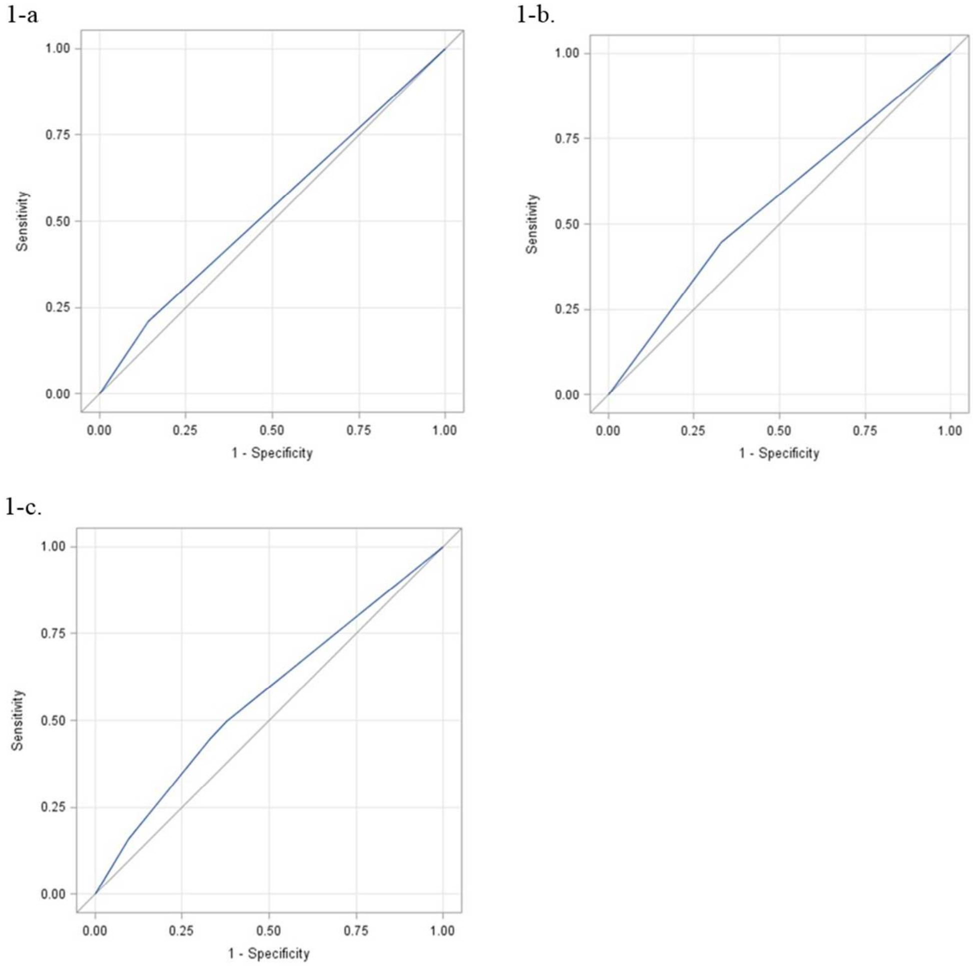
Figure 1. Comparisons of Receiver Operating Characteristic (ROC) curves among BMI only, %BF only and Combined form of BMI and %BF

Footnote.

1-a. ROC curve for %BF only (AUC=.5342)

1-b. ROC curve for BMI only (AUC=.5571)

1-c. ROC corve for Combined form of %BF and BMI (AUC=0.5663)



1-a. ROC curve for %BF only (AUC=.5342)
1-b. ROC curve for BMI only (AUC=.5571)
1-c. ROC corve for Combined form of %BF and BMI (AUC=0.5663)

89x88mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 15
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	7, 16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8,9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The informational value of percent body fat with body mass index for the risk of abnormal blood glucose: a nationally representative cross-sectional study

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ABSTRACT

Objective: To examine the value of percent body fat (%BF) with BMI to assess the risk of abnormal blood glucose (ABG) among US adults who are normal weight or overweight. We hypothesized that normal weight population with higher %BF is more likely to have ABG.

Design: A cross-sectional study.

Setting: National Health and Nutritional Examination Survey (NHANES), 1999–2006, conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention.

Participants: Participants were US adults aged 40 and older who have never been diagnosed with type 2 diabetes by a doctor (unweighted N=6335, weighted N=65705694). The study population was classified into four groups: 1) normal weight with normal %BF, 2) normal weight with high %BF, 3) overweight with normal %BF and 4) overweight with high %BF.

Main outcome measures: Odds ratios for ABG including prediabetes and undiagnosed diabetes (HbA1c≥5.7%, ≥39 mmol/mol).

Results: 64% of population with normal BMI classification, had a high %BF . Prevalence of ABG in normal weight group with high %BF (13.5%) is significantly higher than the overweight group with lower %BF (10.5%, p<.001). In an unadjusted model, the odds ratio of ABG was significantly greater in adults at normal BMI with high %BF compared to individuals at normal weight with lower %BF. In an adjusted model controlling for age, sex, race/ethnicity, first degree of relative diabetes, vigorous-intensity activities and muscle strengthening activities, risks of ABG were greater in population with normal weight and high %BF (OR, 1.55, 95% CI, 1.01-2.38) and with overweight and low %BF(OR, 1.17, 95% CI, 0.69-1.98, p<.05).

Conclusions: Integrating BMI with %BF can improve in classification to direct screening and prevention efforts to a group currently considered healthy and avoid penalties and stigmatization of other groups that are classified as high risk of ABG.

Keywords: abnormal glucose, diabetes prevention, percent body fat, body mass index

Strengths and limitations of this study

- The study used population-based nationally representative data allowing for generalizability.
- We used the most accurate body composition measurement, DXA to assess direct impact of high body fat on abnormal blood glucose.
- Percent body fat integrating with BMI improved classification of population who has high body fat associated with high risk of abnormal blood glucose.
- The data is relatively old while it is the most recent data including whole body DXA measurement.
- There is no gold standard cut off points in defining obesity according to percent body fat.

Introduction

Diabetes has become a worldwide epidemic. It is one of leading causes of morbidity and mortality in the US and its prevalence has been steadily increasing (1, 2). The prevalence of diagnosed diabetes reached to 12.3% of US adults in 2011-2012 (1). Furthermore, the total direct medical costs for diabetes was $176 billion in 2012 and health care expenditure for people with diabetes is more than 2 times higher than people without diabetes (3).

In an effort to prevent diabetes and identify patients with undiagnosed diabetes for potential treatment, the United States Preventive Services Task Force (USPSTF) recommends screening of abnormal blood glucose (prediabetes or undiagnosed diabetes) for asymptomatic adults (4, 5). The USPSTF recommends screening adults aged between 40years old and 70 years old only if they are overweight or obese defined by body mass index (BMI) cutoffs (4). Recently, the Equal Employment Opportunity Commission (EEOC) proposed the rule that if employees who are overweight or obese fail to achieve a normal weight (18.5-24.9kg/m^2) through wellness programs, they penalize the employees who participate into wellness program up to 30% of the total costs of health insurance (6). Consequently, BMI levels have substantial implications for defining someone as low risk of ABG or high risk of ABG.

BMI which is widely adopted to assess obesity-related risk in clinical setting, however, may misclassify some segments of the general population who are at metabolic risk. While BMI is a simple equation based on height and weight, body weight that includes not only body fat but also muscle, bone and body water (7). Recent studies found that half of people who were obese according to percent body fat (%BF) but were classified as normal weight defined by BMI, and about 18% of adults with high %BF who were classified as not being obese showed a significant higher prevalence of metabolic syndrome (8, 9). Recent data indicates that a significant proportion of people with a normal weight designated by BMI (18.5-24.9 kg/m^2) have prediabetes, undiagnosed diabetes and hypertension (10-12). In fact, 33% of adults 45 years old and older at a normal weight have prediabetes. Moreover, a normal weight obesity (NWO) which represents an individual who fall into normal range of BMI and who have high body fat mass is associated with higher risk of metabolic syndrome, cardiometabolic dysregulation and cardiovascular mortality (13, 16). On the other hand, professional football players who are

typically classified as being obese due to high muscle mass actually showed better cardiovascular health compared to the general population (17).

Because of the possible deleterious consequences due to BMI misclassification, percent body fat (%BF) may have some value as an addition to BMI to improve classification of individuals as low risk of ABG or high risk of ABG (14, 15, 18). However, the extent to which adding %BF to BMI improves classification of risk is unclear. There has been little investigation to determine the incremental value of combining BMI and %BF in a risk assessment for abnormal blood glucose. Therefore, the purpose of this study is to examine in a nationally representative sample the value of %BF with BMI to assess the risk of abnormal glucose among adults who are normal weight or overweight and improve classification.

Methods

We analyzed the nationally representative, National Health and Nutrition Examination Survey (NHANES) for the years of 1999-2006. Although there are more recent NHANES data, this is the most recent data with a whole body Dual-energy X-ray Absorptiometry (DXA) which measures %BF. The NHANES is a national representative survey of noninstitutionalized US population using a complex stratified multistage probability cluster sample design. To account for nationally representative population estimates, the National Center for Health Statistics (NCHS) applies a multilevel weighting system. The survey included a standardized medical examination including blood and urine analysis for examining biomarkers and a number of health-related interviews. The current study was approved as exempt by the Institutional Review Board (IRB) at the University of Florida.

Anthropometric Assessment

BMI was obtained from body weight divided by height squared (kg/m^2). Weight and height were measured by a trained examiner in the mobile examination center and these were used to calculate BMI (19). BMI values were categorized into four groups (i.e., underweight, normal weight, overweight and obesity) on the basis of guideline of the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) (7). Percent body fat (%BF) was derived from 1-3 times weekly measured whole body DXA scan (Hologic, Inc., Bedford, Massachusetts) (20). A sex-specific threshold of %BF was adopted as

25% for men and 35% for women given by the AACE/ACE guideline (Obesity in men ≥25% and women ≥35%) (7).

Participants

The current study focused on adults aged over 40 years old or older who have never been told by a doctor or a health professional that they have diabetes (unweighted n=6,335). We focused on individuals 40 years old and older since 40 years old is the lower age cutoff for screening for abnormal blood glucose as suggested by the USPSTF(4). The study population was individuals with normal weight or overweight as defined by BMI. We limited the study to these individuals because they were the groups most likely to potentially be classified by the addition of %BF to BMI.

Participants were limited to normal weight and overweight population (18.5-29.9 kg/m^2) and classified as four groups based on combined BMI and %BF. Respondents who were underweight and obesity defined by BMI were excluded (missing N=5,744). In normal BMI (18.5-24.9 kg/m^2), the first group who had normal BMI and low %BF would be assessed to be at low risk. The second group may be classified as low risk of ABG even though existing data suggests a substantial population have prediabetes (normal BMI but high %BF) (12). Among individuals classified as overweight by BMI (25-29.9 kg/m^2), the third group may be classified as high risk of ABG, but they may be healthy due to the BMI limitation of not appropriately assessing extensive muscle mass (overweight and low %BF). The fourth group would be at high risk based on having high fat (overweight and high %BF). Pregnant women who were not allowed to test the DXA examination were excluded. Also we excluded the obese population because of the known high risk.

Outcomes

The primary outcome is an abnormal glucose including prediabetes or undiagnosed diabetes, an HbA1c level of 5.7% or higher (≥39mmol/mol). All subjects reported never having been told by a doctor or a health professional that they had prediabetes or diabetes (5). We excluded individuals with an HbA1c of 4.0% (≤20 mmol/mol) that is associated with increased mortality without diabetes (21).

Covariates

Age was classified into two groups with cut offs of 40 years old and 71 years old. Race/ethnicity was categorized into four groups, 1) Non-Hispanic White, 2) Non-Hispanic Black, 3) Hispanics and 4) Other. Family history is a predictor of diabetes according to preliminary study (22). Thus we selected family history of diabetes representing a first degree of relative ever being told by a health professional that they had diabetes.

We also assessed physical activity. Intense activity helps to increase muscle mass and reduce body fat and it may result in overweight despite low %BF. Also physical activity represents a lifestyle intervention to control blood glucose. Vigorous activity was defined as reports of an activity that causes a slight to moderate increase in breathing or heart rate for at least 10 minutes over the past 30 days. Muscle strengthening activity refers to any physical activities designed to strengthen muscles including lifting weights, push-ups or sit-ups over the past 30 days.

Statistical Analysis

To account for the stratified multistage probability sample design, we used SAS 9.4 (Cary, NC) and SUDAAN software (RTI, NC) for data analyses. Weighting and design variables applied to all analyses from univariate analyses, chi-square tests and logistic regression models. They allow us to estimate population estimates for noninstitutionalized US population. We examined bivariate relationship between combined BMI/%BF and abnormal glucose. Following by, both unadjusted and adjusted logistic regressions controlling for age, sex, race/ethnicity, family history of diabetes, vigorous activity and muscle strengthening activity was employed to assess likelihood of having abnormal blood glucose.

Patient and Public Involvement

Patients and/or public were not involved in this study.

Results

The total unweighted sample size was 6,335 US adults representing 65,705,694 adults in the US population. No variable had more than 3% unweighted missing data and none of the demographics had any missing data. It is important to note that the population estimates are based on weighted sample. Table 1 showed that among normal weight population, approximately 64% of population of normal BMI classification had a high %BF. Prevalence of abnormal glucose by combined BMI and %BF is shown in Table 2. Prevalence of abnormal blood glucose in the normal weight group with high %BF (13.5%) is significantly higher than the overweight group with lower %BF (10.5%) (p<.001). About 78% of the study population was adults aged between 40 years old to 70 years old and Non-Hispanic White. In sex, most men showed low %BF whereas more than 70% of women has a high level of a body fat within normal weight population. Regardless of BMI, more than 40% of the study population with low %BF performed vigorous-intensity activity as well as muscle strengthening activity compared to population with high %BF (p<.001).

In an unadjusted logistic regression, the odds ratio of abnormal glucose was significantly greater in adults at normal weight with high %BF compared to individuals at normal weight with low %BF as the reference group (Table 3). Conversely, abnormal blood glucose risk was not significantly more likely in overweight adults with low %BF when compared to the normal weight/low %BF group. In an adjusted model controlling for age, sex, race/ethnicity, first degree of relative diabetes, vigorous-intensity activities and muscle strengthening activities, the adjusted model results were similar to the unadjusted results. Risks of abnormal blood glucose were greater in population with normal weight and high %BF as well as the overweight with high %BF (Table 3).

In sensitivity analyses, Area Under the Curve (AUC) of combined form of BMI and %BF was larger than areas of BMI only or %BF only (Figure 1). These areas were significantly different (p<.001).

Discussion

The use of BMI only may misclassify segments of the adult population in terms of risk of abnormal glucose. Our key findings showed that individuals with normal weight who have high percent body fat (%BF) have significantly higher risk of abnormal glucose compared with individuals with normal weight and low %BF. Conversely, of individuals with overweight, low %BF is not significantly associated with the risk of abnormal glucose. The results suggest that %BF combined with BMI may help to improve risk stratification for abnormal blood glucose in these intermediate groups.

Since body weight comprises not only fat but also a variety of body compositions such as muscle, organs and body water, it may not estimate actual amount of body fat. Professional football players who are typically classified as obesity due to high muscle mass showed better cardiovascular health compared to general population (17). In addition, among military population, whereas an average of BMI was overweight, almost half of them had never had any form of sickness absence (23). Furthermore, since according to our preliminary study, 33% of normal weight population has prediabetes, %BF may identify this normal weight population at risk of development of ABG (11). These evidences indicate that %BF may be a key factor in improving to estimate risk of chronic disease.

Our key findings may suggest refinement of current clinical guidelines with additional body composition assessments. The USPSTF and the American Diabetes Association (ADA) have BMI as a key component of recommendations for diabetes prevention (4, 5). There may be missed opportunities for screening, particularly for prediabetes. Regardless of BMI, people with high %BF were older, female and Non-Hispanic White. While the proportion of family history patients with a positive for diabetes was similar across four groups, physical activity was different among groups. It is particularly important, as shown in our findings, that we appropriately classify the overweight population with low %BF. This population has been neglected as being classified as a healthy population. Our finding showed that these individuals are significantly more likely to perform high-intensity physical activities compared to the normal weight population who had low %BF and this behavior may result in overweight. For instance, professional athletes or civil forces with higher muscle mass who are typically classified as obesity measured by BMI may fail to meet normal BMI criteria in recruitment screening (24). In addition, according to the rule offered by EEOC, employees who are classified as overweight or obesity with high muscle mass and lower body fat may get penalized (6). Our findings indicated that BMI may not be the optimal tool to assess health outcomes for employees and new rule of the EEOC should be modified to consider body fat instead of body weight. Using a concept of normal weight obesity has also an opportunity to better detect population at risk of abnormal blood glucose to receive appropriate prevention services. This strategy may detect more than

303,000 US adults who are normal weight and who usually miss an opportunity to receive preventive care service on time due to the use of BMI only. To prevent these adverse events, more accurate body composition assessment may be required.

A direction for future research might be to refine the cut points for %BF, particularly in a longitudinal cohort. Further, it may be important to consider some other variables that may confound the relationship between %BF and diabetes like poverty, diet quality, smoking, and sleep (25, 26). In particular, these variables may be important for future interventions.

Limitations

There are limitations to this study. First, there is no gold standard clinical cut point to indicate high or low percentage body fat. While numerous studies used a variety of sex-specific thresholds, sensitivity analysis has not been implemented yet. The current study however, adopted commonly used criteria as a way to promote generalizability and comparability to other studies. Second, although this is a study investigating the association between several physiological measures, the data is not the most recent NHANES and so population estimates may not totally represent the current US population. While there are more recent NHANES data, the data used in the study is the most recent data with a whole body DXA measurement. We felt that the validity of the DXA scan for %BF was a strength that outweighed the recent data collection. Third, our analyses were cross sectional and did not allow us to look at the downstream risks of individuals with normal weight obesity. However, our primary goal was to improve on BMI in the accuracy of screening guidelines for individuals with current abnormal blood glucose which thereby requires cross-sectional analyses. Lastly, the use of a DXA scan may be an economic burden in health care setting. While a DXA scan is the most accurate technique to measure body compositions, it is prohibitively expensive to use for the purpose of screening only. Current insurance company does not cover the use of DXA scan for the purpose of screening of chronic diseases. Bioelectrical Impedance Analysis (BIA) which assesses %BF may be a cost-effectiveness alternative for the purpose of ABG screening in primary care setting, while current study used the data measured by DXA scan.

Conclusion

BMI which is typically used to define normal weight or overweight in a clinical setting may misclassify populations in relation to abnormal blood glucose. Integrating BMI with %BF can help in classification to direct screening and prevention efforts to a group currently considered low risk of ABG and avoid penalties and stigmatization of other groups that are classified as high risk of ABG.

Acknowledgments

Contributors:

Ara Jo, PhD led the entire research as the first author from writing the manuscript, analyzing the data and interpretation.

Dr. Arch G. Mainous III, PhD supervised the entire process of the research as a research mentor and contributed to writing the manuscript.

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Ethics approval: This study was approved as exempt by the Institutional Review Board at the University of Florida.

Data sharing statement: Data are available through the National Health and Nutrition Examination Survey access from https://www.cdc.gov/nchs/nhanes/index.htm.

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Table 1. BMI Classification among US Adults aged over 40 or older who are Normal weight and Overweight Stratified by BMI and %BF (Unweighted N=6,335 and Weighted N=65,705,694)

		BMI (kg/m^2)	
		Normal (18.5-24.9 kg/m^2)	Overweight (25.0-29.9 kg/m^2)
%BF	Low	36.3	9.0
	High	63.7	91.0

Table 2. Baseline characteristics of adults aged over 40 or older who are normal weight and overweight (Unweighted N=6,335 and Weighted N= 65,705,694)

Body Mass Index	Normal		Overweight		p-value
% of Body Fat	Low	High	Low	High	
Unweighted Sample Size	908	1679	327	3421	
Weighted Sample Size	10259138	18020486	3382474	34043596	
Prevalence of Abnormal Blood Glucose	8.6	13.5	10.5	20.0	<.001
Age					
40 to 70	92.3	81.1	96.0	85.2	<.001
71 or older	7.7	18.9	4.0	14.8	
Sex					
Men	61.1	28.8	96.2	53.4	<.001
Women	38.9	71.2	3.8	46.6	
Race					
Non-Hispanic White	77.5	80.4	70.4	77.0	<.001
Non-Hispanic Black	11.7	4.8	17.0	8.0	
Hispanics	6.5	7.1	10.0	10.9	
Others	4.3	7.7	2.6	4.2	
First Degree Relative Diabetes					
Yes	35.9	45.5	43.6	46.9	<.001
No	64.2	54.5	56.4	53.1	
Vigorous Activity					
Yes	41.7	28.1	45.9	30.4	<.001
No	58.3	71.9	54.1	69.6	
Muscle Strengthening Activities					
Yes	40.5	25.1	38.1	23.4	<.001
No	59.5	74.9	61.9	76.7	

Table 3. Odds Ratios (95% Confidence Intervals) for the Abnormal Glucose for Adults with Normal Weight and Overweight in Unadjusted and Adjusted Logistic Regression Models controlling for age, sex, race/ethnicity, first degree relative diabetes, vigorous activities, and muscle strengthening activity

BMI	%BF	Unadjusted OR	Adjusted OR
Normal (18.5-24.9kg/m^2)	Low	1.00	1.00
	High	1.66 (1.13-2.43)*	1.55 (1.01-2.38)*
Overweight (25-29.9kg/m^2)	Low	1.25 (0.75-2.07)	1.17 (0.69-1.98)
	High	2.64 (1.86-3.76)*	2.45 (1.61-3.71)*

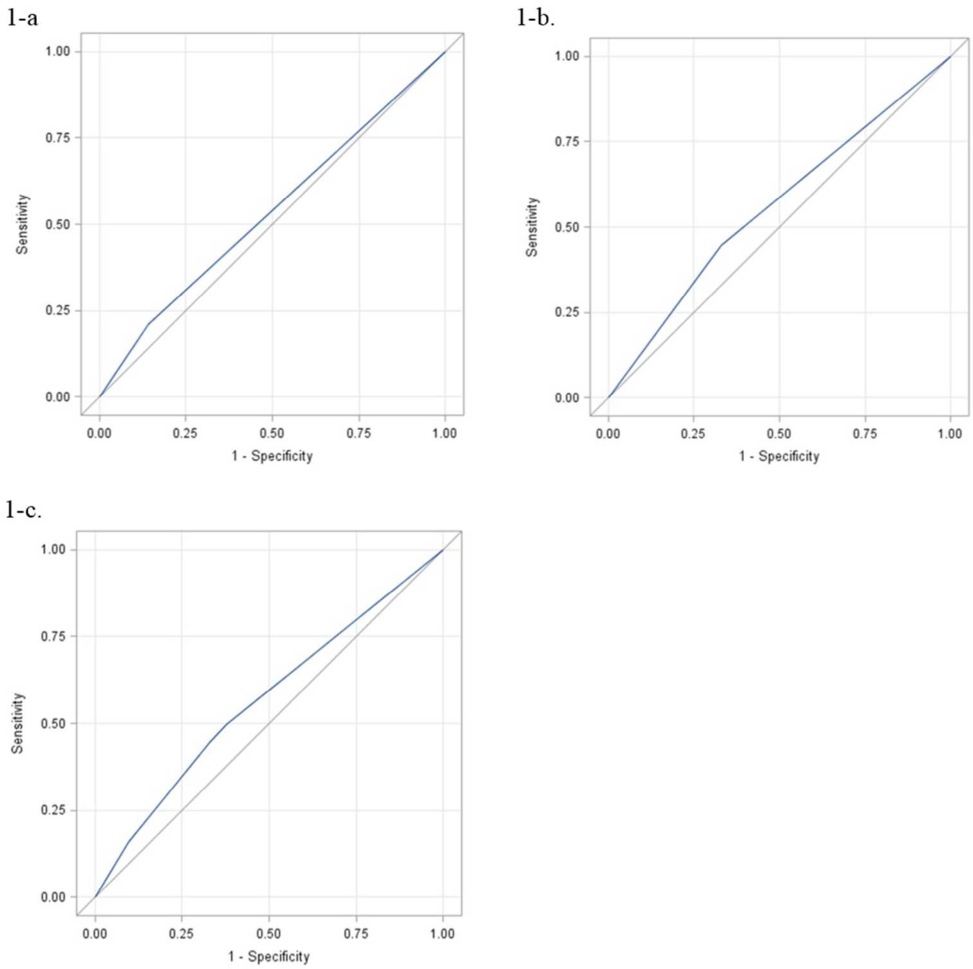
*** statistically significant at .05**

Figure 1. Comparisons of Receiver Operating Characteristic (ROC) curves among BMI only, %BF only and Combined form of BMI and %BF

1-a. ROC curve for %BF only (AUC=.5342)

1-b. ROC curve for BMI only (AUC=.5571)

1-c. ROC corve for Combined form of %BF and BMI (AUC=0.5663)



1-a. ROC curve for %BF only (AUC=.5342)
1-b. ROC curve for BMI only (AUC=.5571)
1-c. ROC corve for Combined form of %BF and BMI (AUC=0.5663)

89x88mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 15
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	7, 16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8,9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.