Does Lean Body Mass Equal Health Despite Body Mass Index?

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ABSTRACT

Objective: To determine the association between having simultaneously high body mass index (BMI) and high relative lean body mass (LBM) and cardio-metabolic risk factors, metabolic syndrome (MetS), and diabetes in adults.
**Materials and Methods:** A cross-sectional analysis was performed on 4982 adults aged 19 to 85 years that participated in the National Health and Nutrition Examination Survey (cycles 1999-2000 to 2005-2006). The primary exposure variable was categorization into four groups: (1) Low-BMI/Low-LBM, (2) Low-BMI/High-LBM, (3) High-BMI/Low-LBM, and (4) High-BMI/High-LBM. LBM was assessed using Dual Energy X-ray absorptiometry. The primary outcome measures were cardio-metabolic risk factors, MetS based on the ATP III definition; participants were required to have at least three of the following five criteria: high waist circumference, low HDL cholesterol, elevated triglyceride levels, high resting blood pressure, and self-reported diabetes.

**Results:** Compared to the High-BMI/High LBM, most cardio-metabolic risk factors were significantly different among groups (p<0.05) while no such differences were observed for the High-BMI/Low-LBM (p>0.05). Exception of waist circumference [OR (95%): 21.8 (8.84-53.82)], there was no increased odds of having cardiometabolic risk factors in the High-BMI/Low-LBM compared to the High-BMI/High-LBM (p>0.05). The odds of having MetS and diabetes for the High-BMI/Low-LBM compared to the High-BMI/High-LBM were OR (95% CI): 1.68 (0.84-3.36) and 0.59 (0.26-1.34) respectively.

**Conclusions:** Our results suggest that having a high BMI as well as high relative LBM levels is not associated with cardio-metabolic risk factors, MetS, and diabetes. Therefore, maintaining a BMI below 30 kg/m² appears to be clinically relevant, regardless of LBM levels.

**INTRODUCTION**

The World Health Organization (WHO) estimated that the number of individuals living with obesity has doubled worldwide over the last thirty years\(^1\). In fact, the WHO estimated that about 39% of adults aged 18 years and over are overweight and 13% are living with obesity\(^1\). The high prevalence of overweight and obesity worldwide is concerning from a cardio-metabolic risk factors standpoint. Body mass index (BMI) is used in clinical settings for evidence-based decision making as
it is easy to use, and studies suggest that there is a strong association between BMI and fat mass. In addition, studies suggest an association between BMI and an increase in cardio-metabolic risk factors including high blood pressure, high waist circumference, high blood glucose levels, high triglyceride levels, and decreased high-density lipoprotein, as well as metabolic syndrome and diabetes. In addition, BMI has been associated with cardiovascular disease (CVD), increased premature mortality, and risk of all-cause mortality. In fact, a study observed a 30% higher risk of all-cause mortality for each 5kg/m² increase in BMI. Ortega et al. (2016) investigated different body composition measures and their associations with CVD mortality and all-cause mortality. The results showed that excessive fat mass was significantly associated with CVD mortality and all-cause mortality. Interestingly, total LBM was associated with a 20% increased likelihood of CVD mortality. When accounting for height, LBM index was associated with a 2-fold increase in the risk of CVD mortality, reinforcing the idea that LBM is not always protective. In addition, a study performed by Zhu et al. (2003) showed that fat mass index and LBM index were both associated with premature mortality when using skinfolds. Interestingly, a recent study investigated whether LBM was protective against major cardiovascular events in individuals with pre-established diabetes found that LBM has not protective effect on major cardiovascular events. Nevertheless, these studies are limited by their method of only measuring BMI instead of also accounting for body fat distribution or total lean body mass (LBM) using a gold standard measure.

LBM is the primary site of glucose uptake; and therefore, it has been suggested that LBM protects against cardio-metabolic risk factors and diabetes. Although rational, few studies support that both BMI and high LBM are independently associated with unfavorable cardio-metabolic profiles. For example, a study including 421 men and women suggests that age and LBM (but not fat mass) explained 46% of the unfavorable cardio-metabolic risk factors profile. A prospective study found that total reduction in LBM was not significantly associated with incidence of diabetes. Moreover, even if a meta-analysis found lower LBM levels in individuals with diabetes, this study failed to conclude that LBM was significantly associated with a reduction in the odds of MetS and suggest that this association is uncertain.

Although studies have investigated the association between fat mass and LBM with cardio-metabolic risk factors, there are limited studies investigating the simultaneous contribution of LBM.
and BMI to MetS, and diabetes. This information is relevant as both MetS and diabetes has been associated with CVD, cancer, and all-cause mortality\textsuperscript{13,14} and better insight into these factors might help provide more efficient interventions. Therefore, this study investigated the combined effect of high BMI and high LBM on cardio-metabolic risk factors, specifically metabolic syndrome (MetS) and diabetes, in a large sample of adults. The purpose of the current study was to investigate adults with simultaneously high BMI and high LBM and discover the association with cardio-metabolic risk factors, MetS, and diabetes. We hypothesized that no difference would be observed between individuals with a high BMI and high LBM, and individuals with high BMI and low LBM regarding their likelihood of having MetS or diabetes.
MATERIALS AND METHODS

Study population

The study sample consisted of 4982 men and women aged between 19 and 85 years old who participated in the 1999-2000 to the 2005-2006 National Health and Nutrition Examination Survey (NHANES), which was designed to represent the United States population. To produce reliable statistics, NHANES over-samples persons 60 and older, African Americans, and Hispanics. From the 30,273 individuals included in the original sample, 3014 were excluded due to missing data for body composition. In addition, 19784 were excluded due to being outside of the sample age range (below 19 years of age) which was chosen to encompass an adult population. The remaining sample size was 7475 participants, from which 2493 were excluded because the exposure variable for these individuals was in the second tertile of LBM. The final sample size included in the analysis was 4982 participants and was limited to participants with all the measurements for the primary exposure variables (BMI and LBM) and the primary outcome (cardiometabolic risk factors) (Figure 1).

NHANES subjects were identified using a stratified multistage probability sampling design. Detailed survey operation manuals and consent forms are available on the NHANES website. Briefly, NHANES consisted of a home interview and a thorough health examination. During the interview, participants were asked questions about their health status, disease history, and lifestyle behaviors. The health examination was performed in a mobile exam center by a trained investigator and physician. All participants provided written and informed consent. The National Center for Health Statistics approved the protocol.

Anthropometrics

The BMI for each subject was derived from the body composition data set on the NHANES website. The subjects’ BMI were calculated by dividing their weight in kilograms (kg) by the square of their height in meters (m²). For body weight, participants were instructed to stand on the center of a Toledo® digital scale while wearing a gown with paper pants and slippers. Participants were asked to stand with their feet close together with their arms at their sides. Weight was recorded to the nearest 0.01 kg. For height, the participants were instructed to stand on a stadiometer with an adjustable headboard. Participants were instructed to keep their heels touching and their feet pointing approximately 60 degrees outward. There were four points of contact with the stadiometer: heels,
buttocks, shoulder blades and head. While looking straight forward, the participants were instructed to
perform a deep inhale and then the measurement was taken. Height was recorded to the nearest 0.1
centimeter (cm).

Waist circumference was measured from the right side of the body. The examiner palpated the
participant for the right iliac crest and marked a horizontal line above the landmark. In addition, the
examiner marked a vertical line along the midaxillary line. The tape measure was wrapped around the
participant with the bottom of the tape flush with the horizontal line. The measurement was recorded
to the nearest 0.1 cm. More information on how the anthropometric data was collected is available in
the Anthropometric Standardization Reference Manual and can be further examined on the NHANES
website. For the anthropometric measures, each participant was not assessed by the same
individuals; however, NHANES had a group of assessors that were highly trained.

Body Composition

Body composition was measured by dual-energy x-ray absorptiometry (DXA) with a Hologic
QDR-4500A fanbeam densitometer using software version 8.26 (Hologic, Inc., Bedford, MA). A
certified radiology technologist performed the DXA examinations on the participants. DXA provides
validated total and regional measures of fat mass, bone mass, and LBM in all age groups. For the
purposes of the current study, the measurements for total body fat mass and total LBM excluding
bone mineral content were used. For missing data, multiple data imputations were performed
according to the NHANES protocol. The specific protocols for the body composition measurements
can be found on the NHANES website.

Primary outcome measures

Metabolic syndrome: The National Cholesterol Education Program Adult Treatment Panel
III MetS definition was used. This definition of MetS includes high waist circumference (women: ≥
88 cm; men: ≥ 102 cm), low HDL-cholesterol (women: ≤1.30 mmol/L; men: ≤ 1.04 mmol/L), elevated
triglyceride levels (women and men: ≥ 1.7 mmol/L), high resting blood pressure (women and men:
≥130 mmHg / 85 mmHg) and high fasting glucose levels (women and men: ≥ 5.6 mmol/L).
Individuals with at least three of the five cardio-metabolic risk factors listed above were considered to
have MetS. Serum and plasma were collected in the mobile examination center following a period of
8.5 hours of fasting. Plasma specimens were processed, stored, and shipped to the Johns Hopkins
University Lipoprotein Analytical Laboratory for analysis. Blood pressure was manually measured by a physician that was previously certified for blood pressure evaluation based off the Shared Care Research and Education Consulting. Participants were asked to sit with their feet flat on the floor for five minutes prior to the measurement with their back and arms supported by the chair. The average of three consecutive measurements were taken with 30 seconds breaks between each measurement.

Secondary outcome measure

Self-reported diabetes: Diabetes was self-reported via questionnaire. Participants were asked, “Have you ever been told by a physician or a health professional that you had diabetes?” A score of 1 was given when individuals answered positively.

Primary exposure variable

Given that 1) LBM decreases with aging and 2) LBM is significantly different between men and women, a linear regression model, stratified by sex, was used to obtain relative LBM values (absolute total LBM divided by body weight) and these values were adjusted for age of each participant. Thereafter, sex-specific tertiles of relative LBM were created. Individuals in the lowest tertile of relative LBM were considered as Low-LBM, while those in the third tertile were considered High-LBM. Participants in the second tertiles of relative LBM were excluded to target the aim of this study.

Individuals were categorized as having low or high fat mass based on BMI. Individuals were considered as Low-BMI if BMI <30 kg/m², while individuals were considered as High-BMI if BMI ≥30 kg/m². Cut-points for BMI were selected based on the levels where cardio-metabolic risk factors increase significantly. Thereafter, individuals were classified into four groups based on BMI and age-and-sex specific relative LBM tertiles. Individuals were classified into four groups based on BMI thresholds (1) Low-BMI/ Low-LBM, (2) Low-BMI/High-LBM, (3) High-BMI/Low-LBM, and (4) High-BMI/High-LBM

Confounding variables

Covariates: Included in the analyses were age (continuous variable), sex, ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and other), and daily alcohol consumption. Alcohol intake was calculated as follows: non-drinker, light drinker (<1 drink/day), moderate drinker (1-2 drinks/day), and heavy drinker (>2 drinks/day).

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**Food habits:** Total daily energy intake (kcal/day) and quality of food habits were assessed using a 24-hour food recall. A diet’s quality was based on adherence to the *United States Department of Agriculture’s* recommendations\(^\text{25}\) for three main macronutrients: proteins (10-35% of total calories), carbohydrates (40-45% of total calories), and total fat (20-35% of total calories). A score of 1 was given when meeting the recommendation for each nutrient. Then, the number of recommendations met was computed to create a diet quality index with values ranging from 0 to 3. This strategy has been previously used for the same NHANES cycles\(^\text{26}\).

**Statistical analysis**

Data are presented as unadjusted mean ± SD and incidence N (%) for categorical variables unless otherwise stated. A one-way ANOVA was used to identify differences among groups for continuous variables. A Chi-square test was used to assess differences for categorical variables among groups. General linear models were used to quantify the independent association between continuous cardio-metabolic risk factors and the exposure group categories. Bonferroni post-hoc analyses were used to identify any group differences. An interaction variable between BMI and LBM was tested and found to be significantly associated with the primary outcomes (p< 0.05). Logistic regression models were used to investigate the association between the composite High-BMI/High-LBM with cardio-metabolic risk factors. The High-BMI/High-LBM was chosen as the reference group because we were interested in investigating the differences between the two high BMI groups. Age, sex, ethnicity, and alcohol intake were used as covariates in the analyses. Data management and statistical analyses were performed using SPSS version 20 and SAS software, Version 9.4 of the SAS, © 2012, System for Windows (SAS Institute Inc., Cary, NC, USA). A p≤0.05 was considered significant. Statistics final models accounted for the sample weights and complex survey design (strata, probability sampling units). However, the descriptive data was not weighted.
RESULTS

A significant difference was observed among groups for age, ethnicity ($p<0.001$), sex ($p=0.049$) and alcohol consumption (Table 1; $p<0.001$). A significant difference among groups was also observed for waist circumference ($p=0.001$), BMI ($p<0.001$), total fat mass ($p=0.008$), and LBM ($p<0.001$). No significance differences were observed between groups for dietary intake ($p>0.05$). As for cardio-metabolic risk factors, MetS, and diabetes, all variables were significantly different among groups ($p<0.05$).

General linear models were performed to quantify differences among groups’ cardio-metabolic risk factors using relative LBM and adjusting for confounders (Table 2). Compared to the High-BMI/High-LBM, all groups were significantly different for waist circumference (all $p<0.001$). In addition, fasting blood glucose and systolic blood pressure were significantly different in the Low-BMI/Low-LBM and the Low-BMI/High-LBM compared to the High-BMI/High-LBM ($p < 0.05$). Triglycerides and systolic blood pressure were significantly lower in the Low-BMI/High-LBM ($p<0.05$) compared to High-BMI/High-LBM, while HDL-cholesterol was significantly higher in the Low-BMI/High-LBM compared to the High-BMI/High-LBM group ($p<0.05$).

Table 3 describes the odds of having cardio-metabolic risk factors in relation to group categorization. Low-BMI/Low-LBM was not associated with a reduced odds of cardio-metabolic risk factors compared to High-BMI/High-LBM ($p> 0.05$). Compared to High-BMI/High-LBM, individuals in the Low-BMI/High-LBM group had a reduced likelihood of having cardio-metabolic risk factors by 56-98%. Except for waist circumference, OR: 21.8 95%CI (8.84-53.82), the High-BMI/Low-LBM was not associated with an increased likelihood of cardio-metabolic risk factors ($p> 0.05$) when compared to High-BMI/High-LBM. Similar results were observed for the odds of MetS (OR: 1.68, 95%CI (0.84-3.36) and diabetes: OR: 0.59, 95%CI (0.26-1.34)) (Figure 2A,B).

DISCUSSION

The main objective of the current study was to investigate the association between having simultaneously high BMI and high LBM and the likelihood of having cardio-metabolic risk factors,
MetS, and diabetes in adults. In particular, we were interested in comparing the likelihood of having cardio-metabolic risk factors in the High-BMI/Low-LBM and High-BMI/High-LBM group. The main result of this study was the lack of significant differences between the High-BMI/Low-LBM and the High-BMI/High-LBM groups for most of the cardio-metabolic risk factors, MetS, and diabetes. These findings challenge the popular belief that BMI is a poor clinical tool because it does not take into consideration LBM. In other words, despite having high LBM, having a BMI $\geq 30$ kg/m$^2$ is associated with the same odds of cardio-metabolic risk factors, MetS, and diabetes.

In the present study, the High-BMI/Low-LBM group was not at an increased likelihood of various cardio-metabolic risk factors or MetS compared to the High-BMI/High-LBM group when using relative LBM. These findings aligned with the study performed by Ortega et al. (2016) who prospectively observed an increased risk of premature mortality in a group of high BMI [HR: 2.7 (95%CI 2.1-3.3)] and a group of high relative LBM [HR: 2.2 95%CI (1.7-2.7)]. Our results expand on the previous study by investigating the additive effect of BMI and high LBM, and by investigating a variety of cardio-metabolic risk factors, as well as MetS and diabetes. Contrary to our findings, a prospective study of 21 years observed a reduced risk of mortality in men with higher levels of LBM (HR: 0.72 95%CI: 0.54-0.96). Although these analyses were adjusted for confounders including BMI, they were performed in a population of older adults (>65 years). This is not trivial and could explain the observed differences as it is established in the literature that older adults face an obesity paradox and suggest that despite a high adiposity level, these individuals are at lower risk of premature mortality. For example, in a meta-analysis of 28,209 individuals living with either overweight or obesity, it was reported that there was a reduced risk of heart failure by 19% and 40%, and a reduced risk of all-cause mortality by 16% and 33% respectively. The discrepancy between our results and other studies might be a reflection of different methodologies used to quantify body composition. For example, in our study we used DXA whereas Graf et al. (2015) used bioimpedance, which has been shown to be affected by the level of hydration, and older adults often have low hydration levels.

In the current study, we did not observe an increased likelihood of diabetes in the High-BMI/Low-LBM group compared to High-BMI/High-LBM group when using relative LBM. This finding is of great interest especially since most believe that having high LBM and a high BMI
reduces the number of cardio-metabolic risk factors as well as the risk of diabetes\textsuperscript{31}. The belief that 
LBM reduces the risk of cardio-metabolic risk factors and diabetes comes from a study that suggests 
that skeletal muscle is the main site of glucose uptake, with 85\% of glucose uptake being performed 
by skeletal muscles\textsuperscript{31}. However, our results do not support this claim and suggest that independent of 
the amount of LBM, having a high BMI increases the likelihood of cardio-metabolic risk factors, 
MetS, and diabetes. Recently, a study observed a positive correlation between gains in LBM and 
insulin resistance in women who performed six months of aerobic and resistance exercise training\textsuperscript{32}, 
which suggests that women with greater LBM gain become more insulin resistant. These results have 
been confirmed by other studies which reported that the amount of LBM might not be as protective as 
what we previously observed\textsuperscript{33,34}. In addition, a previous study that investigated women stratified by 
low or high-visceral adiposity and low or high-LBM reported that post-menopausal women with high 
visceral adiposity exacerbate their cardio-metabolic profile when having High-LBM\textsuperscript{35}. These results 
suggest that excessive LBM might contributes to insulin resistance and have an additive effect on 
visceral adiposity. Our results expand on the previous data by using a more significant and 
heterogeneous sample size, by using a clinical tool for adiposity, and by using statistical approaches 
which improve external validity. Therefore, the findings of the current study are important and 
suggest that 1) BMI is a strong predictor of MetS and diabetes, and 2) attention should pertain to 
muscle quality rather than LBM to prevent further cardio-metabolic risk factors, MetS, and diabetes.

\textbf{Strengths and Limitations}

Although the current study provides novelty to the current literature, as well as provides 
important insight on the topic of body composition and its effects on cardio-metabolic risk factors, 
there are some limitations to the study that must be acknowledged. First, the data we used from the 
NHANES database is cross-sectional; therefore, does not follow individuals over time. This impedes 
the ability to conclude any cause and effect relationships. Second, diabetes was self-reported rather 
than objectively measured, which could have impacted our results. Although the current study has 
several limitations, it is strengthened by a much broader population, which increases external validity. 
In addition, the use of a gold standard measure for body composition on a large sample size of adults 
and the use of sample weights in the data analysis to further account for the complexity of the design 
are strengths of the present study.
PERSPECTIVE

Currently, BMI is used to quickly assess an individual’s weight classification to identify the risk of cardio-metabolic risk factors including MetS and diabetes. That being said, the use of BMI has remained controversial considering that the measurement does not take into consideration body composition. The purpose of the current study was to compare individuals with high BMI, but with differing body composition, to determine if there were any differences in the likelihood of having cardio-metabolic risk factors, MetS, and diabetes. The results of the current study suggest that regardless of LBM levels, the likelihood of having cardio-metabolic factors is identical in all individuals that have a high BMI (≥ 30 kg/m²), thus reinforcing the strength of BMI as a clinical tool for the management of obesity and its related cardio-metabolic risk factors. These findings have implication for health practitioners as they provide evidence that BMI, an easy clinical tool, should be used in clinical setting instead of body composition to monitor likelihood of having MetS and diabetes.

CONCLUSION

In summary, individuals living with obesity based on a BMI ≥ 30 kg/m² have no difference in the likelihood of having cardio-metabolic risk factors, MetS or diabetes regardless of LBM levels. Future research should focus on other outcomes variables, such as inflammation, and the potential mechanisms for such association.

ACKNOWLEDGEMENTS

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Figure Legend:

**Figure 1:** Flow chart representing sample selection. NHANES=National Health and Nutrition Examination Survey, DXA= Dual-energy X-ray Absorptiometry, MetS=Metabolic Syndrome, LBM=Lean Body Mass.

**Figure 2A:** Odds of MetS among groups using the High-BMI/High-LBM group as reference. MetS=Metabolic Syndrome, BMI=Body Mass Index, LBM=Lean Body Mass.

**Figure 2B:** Odds of diabetes among groups using the High-BMI/High-LBM group as reference. MetS=Metabolic Syndrome, BMI=Body Mass Index, LBM=Lean Body Mass.
Table 1: General Characteristics Among Groups

<table>
<thead>
<tr>
<th></th>
<th>Low-BMI Low-LBM</th>
<th>Low-BMI High-LBM</th>
<th>High-BMI Low-LBM</th>
<th>High-BMI High-LBM</th>
<th>P-Value</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>45.1 ± 18.3</td>
<td>45.8 ± 20.1</td>
<td>47.7 ± 17.1</td>
<td>53.0 ± 16.2</td>
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</tr>
<tr>
<td>Men n (%)</td>
<td>473 (62.9%)</td>
<td>1259 (51.8%)</td>
<td>811 (46.6%)</td>
<td>25 (41.7%)</td>
<td>0.049</td>
</tr>
<tr>
<td>Non-Hispanic white n (%)</td>
<td>372 (49.5%)</td>
<td>1213 (49.9%)</td>
<td>821 (47.2%)</td>
<td>19 (31.7%)</td>
<td>0.000</td>
</tr>
<tr>
<td>Non-Hispanic black n (%)</td>
<td>66 (8.8%)</td>
<td>603 (24.8%)</td>
<td>387 (22.3%)</td>
<td>26 (43.3%)</td>
<td></td>
</tr>
<tr>
<td>Non-drinker n (%)</td>
<td>291 (38.7%)</td>
<td>943 (38.8%)</td>
<td>759 (43.6%)</td>
<td>23 (38.3%)</td>
<td></td>
</tr>
<tr>
<td>Moderate drinker (1-2 drinks/day) n (%)</td>
<td>268 (35.6%)</td>
<td>923 (38.0%)</td>
<td>639 (36.7%)</td>
<td>24 (40.0%)</td>
<td>0.006</td>
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<tr>
<td>Heavy drinker (&gt;2 drinks/day) n (%)</td>
<td>193 (25.7%)</td>
<td>565 (23.2%)</td>
<td>341 (19.6%)</td>
<td>13 (21.7%)</td>
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**Anthropometrics and Body composition**

<table>
<thead>
<tr>
<th></th>
<th>Low-BMI Low-LBM</th>
<th>Low-BMI High-LBM</th>
<th>High-BMI Low-LBM</th>
<th>High-BMI High-LBM</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumferences (cm)</td>
<td>98.0 ± 8.3</td>
<td>83.4 ± 9.3</td>
<td>114.7 ± 12.4</td>
<td>103.5 ± 7.0</td>
<td>0.000</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.5 ± 1.9</td>
<td>23.0 ± 2.8</td>
<td>36.3 ± 5.2</td>
<td>32.0 ± 1.7</td>
<td>0.000</td>
</tr>
<tr>
<td>Total Fat Mass (kg)</td>
<td>29.0 ± 4.7</td>
<td>17.4 ± 5.0</td>
<td>42.7 ± 10.1</td>
<td>27.6 ± 4.9</td>
<td>0.008</td>
</tr>
<tr>
<td>Lean Body Mass (kg)</td>
<td>51.0 ± 10.9</td>
<td>49.0 ± 11.0</td>
<td>60.3 ± 13.6</td>
<td>62.4 ± 13.1</td>
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**Energy intake**

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<th>Low-BMI Low-LBM</th>
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<th>High-BMI Low-LBM</th>
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<th>P-Value</th>
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<tr>
<td>Total Kcal</td>
<td>2152.9 ± 996.4</td>
<td>2225.2 ± 1082.7</td>
<td>2085.8 ± 991.1</td>
<td>1928.0 ± 1095.8</td>
<td>0.514</td>
</tr>
<tr>
<td>Total Fat (g)</td>
<td>79.7 ± 49.1</td>
<td>81.0 ± 46.8</td>
<td>79.8 ± 46.0</td>
<td>69.6 ± 46.3</td>
<td>0.504</td>
</tr>
<tr>
<td>Total carbohydrate (g)</td>
<td>266.6 ± 121.3</td>
<td>280.2 ± 142.8</td>
<td>255.8 ± 135.8</td>
<td>237.8 ± 138.6</td>
<td>0.534</td>
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<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
<td>Group 3</td>
<td>Group 4</td>
<td>p-value</td>
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<td>-------------------------</td>
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<tr>
<td>Total protein (g)</td>
<td>80.4 ± 43.7</td>
<td>81.2 ± 46.0</td>
<td>79.5 ± 43.0</td>
<td>75.7 ± 56.2</td>
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*Cardio-metabolic risk factors and Chronic diseases*

<table>
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<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.7 ± 1.9</td>
<td>1.3 ± 1.0</td>
<td>1.9 ± 1.8</td>
<td>1.9 ± 1.6</td>
<td>0.000</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/L)</td>
<td>1.3 ± 0.4</td>
<td>1.5 ± 0.4</td>
<td>1.2 ± 0.3</td>
<td>1.3 ± 0.4</td>
<td>0.007</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.7 ± 1.6</td>
<td>5.5 ± 1.6</td>
<td>6.1 ± 2.1</td>
<td>6.5 ± 2.2</td>
<td>0.033</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>124.0 ± 18.8</td>
<td>122.1 ± 20.4</td>
<td>127.5 ± 18.5</td>
<td>135.7 ± 25.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>71.3 ± 13.0</td>
<td>68.8 ± 13.1</td>
<td>73.3 ± 13.0</td>
<td>74.6 ± 14.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Metabolic syndrome n (%)</td>
<td>249 (33.1%)</td>
<td>312 (12.8%)</td>
<td>949 (54.6%)</td>
<td>32 (53.3%)</td>
<td>0.000</td>
</tr>
<tr>
<td>Diabetes n (%)</td>
<td>44 (5.9%)</td>
<td>146 (6.0%)</td>
<td>218 (12.5%)</td>
<td>12 (20.0%)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Data are presented as unweighted mean ± SD and n (%) for continuous and categorical variable respectively and the analysis are weighted. The data was calculated via a one-way ANOVA test for continuous variables and a Chi Square for categorical variables.

Table 2: Association Between Cardio-Metabolic Risk Factors and Group Categories

<table>
<thead>
<tr>
<th>Groups using Relative LBM</th>
<th>Low-BMI</th>
<th>Low-BMI</th>
<th>High-BMI</th>
<th>High-BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low-LBM</td>
<td>High-LBM</td>
<td>Low-LBM</td>
<td>High-LBM</td>
</tr>
<tr>
<td>N= 752</td>
<td>N=2431</td>
<td>N=1739</td>
<td>N=60</td>
<td></td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>96.9 (96.0-97.8)</td>
<td>81.8 (81.2-82.4)</td>
<td>114.0 (113.3-114.7)</td>
<td>100.0 (96.9-103.1) **†‡</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.7 (1.5-1.8)</td>
<td>1.2 (1.1-1.3)</td>
<td>1.8 (1.7-1.9)</td>
<td>1.7 (1.2-2.1)</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/L)</td>
<td>1.4 (1.4-1.4)</td>
<td>1.5 (1.5-1.6)</td>
<td>1.2 (1.2-1.3)</td>
<td>1.4 (1.3-1.5)</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.6 (5.4-5.7)</td>
<td>5.4 (5.3-5.5)</td>
<td>5.9 (5.8-6.0)</td>
<td>6.0 (5.6-6.4) †</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>122.1 (120.6-123.5)</td>
<td>119.3 (118.4-120.3)</td>
<td>125.2 (124.1-126.3)</td>
<td>127.0 (122.2-131.8) †</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>73.8 (72.7-74.9)</td>
<td>70.8 (70.0-71.5)</td>
<td>74.8 (74.0-75.6)</td>
<td>75.0 (71.4-78.7)</td>
</tr>
</tbody>
</table>

The results are presented as least square means (95% CI). The data was analyzed using a univariate general linear model and are weighted. The model adjusted for age, sex, ethnicity, and alcohol intake. The reference group was the High-BMI High-LBM group. LBM=Lean Body Mass, BMI=Body Mass Index, HDL=High-Density Lipoprotein, BP=Blood Pressure. * Represents significance for Low-BMI/Low-LBM, † Represents significance for Low-BMI/High-LBM, ‡ Represents significance for High-BMI/Low-LBM; All p-value ≤ 0.05.
<table>
<thead>
<tr>
<th>Groups using Relative LBM</th>
<th>N= 752</th>
<th>N=2431</th>
<th>N=1739</th>
<th>N=60</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Waist circumference</td>
<td>0.50 (0.22-1.14)</td>
<td>0.02 (0.01-0.03)</td>
<td>21.8 (8.84-53.82)</td>
<td>Ref</td>
</tr>
<tr>
<td>High Triglycerides</td>
<td>0.92 (0.45-1.87)</td>
<td>0.34 (0.17-0.68)</td>
<td>1.25 (0.62-2.52)</td>
<td>Ref</td>
</tr>
<tr>
<td>Low HDL-cholesterol</td>
<td>0.62 (0.29-1.31)</td>
<td>0.30 (0.15-0.63)</td>
<td>1.00 (0.48-2.06)</td>
<td>Ref</td>
</tr>
<tr>
<td>High Glucose</td>
<td>0.60 (0.29-1.23)</td>
<td>0.34 (0.17-0.69)</td>
<td>1.18 (0.58-2.38)</td>
<td>Ref</td>
</tr>
<tr>
<td>High Systolic BP</td>
<td>0.65 (0.29-1.45)</td>
<td>0.44 (0.20-0.97)</td>
<td>0.86 (0.39-1.90)</td>
<td>Ref</td>
</tr>
<tr>
<td>High Diastolic BP</td>
<td>0.65 (0.28-1.54)</td>
<td>0.41 (0.18-0.95)</td>
<td>1.00 (0.44-2.29)</td>
<td>Ref</td>
</tr>
</tbody>
</table>

The results are presented as odd ratios (OR) and 95% confidence intervals (CI). The data was analyzed using a binary logistic regression, are weighted, and the reference group was the High-BMI High-LBM. The model adjusted for age, sex, ethnicity, and alcohol intake. LBM=Lean Body Mass, BMI=Body Mass Index, HDL=High-Density Lipoprotein, BP=Blood Pressure. All p-value ≤ 0.05.
A

Odds of MetS

- High-BMI/Low-LBM: 1.68 (0.84-3.36)
- Low-BMI/High-LBM: 0.12 (0.06-0.25)
- Low-BMI/Low-LBM: 0.55 (0.27-1.12)

B

Odds of Diabetes

- High-BMI/Low-LBM: 0.59 (0.26-1.34)
- Low-BMI/High-LBM: 0.20 (0.09-0.47)
- Low-BMI/Low-LBM: 0.21 (0.20-0.52)