Association of Lipopolysaccharide-Binding Protein With Aging-Related Adiposity Change and Prediabetes Among African Ancestry Men

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OBJECTIVE

Cross-sectional studies suggest that lipopolysaccharide-binding protein (LBP) may be associated with obesity and metabolic disorders. However, prospective studies examining LBP are lacking. This prospective study investigated the association between LBP and metabolic abnormalities in 580 African ancestry men (mean age, 59.1 ± 10.5 years).

RESEARCH DESIGN AND METHODS

We measured fasting serum LBP at baseline. Changes in adiposity and glucose homeostasis as well as case subjects with new type 2 diabetes and impaired fasting glucose (IFG) were assessed at a follow-up visit ~6 years later. Baseline LBP values were tested across quartiles for linear trend with metabolic measures. Multivariable logistic regression was used to determine the odds of new cases of IFG or diabetes per 1-SD greater baseline LBP.

RESULTS

LBP was significantly associated with baseline BMI, waist circumference, whole-body and trunk fat, skeletal muscle density, fasting serum insulin, and HOMA-insulin resistance (IR) (all \( P < 0.01 \)). Greater baseline LBP was significantly associated with longitudinal increases in the percentage of trunk fat (\( P = 0.025 \)) and HOMA-IR (\( P = 0.034 \)), but only borderline so with a decrease in skeletal muscle density (\( P = 0.057 \)). In men with normal glucose, baseline LBP was associated with increased odds of having IFG at follow-up after adjustment for age, baseline trunk fat, and lifestyle factors (odds ratio per 1-SD LBP: 1.51; 95% CI 1.02–2.21). This association was attenuated after additional adjustment for change in trunk fat (\( P = 0.067 \)).

CONCLUSIONS

LBP may be a marker of prediabetes. Some of this association appears to be mediated through increased central and ectopic skeletal muscle adiposity.

Diabetes and obesity are associated with low-level, chronic inflammation (1). In recent years, the gut microbiota have come to be recognized as a contributor to this inflammation (2,3). Gram-negative bacteria contain lipopolysaccharide (LPS) in their outer membranes (4), and through their life cycles the bacteria can shed LPS...
LBP Association With Adiposity and Prediabetes

Diabetes Care

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flammation in humans (13,14).

LBP levels are higher among individu-
als who are obese, have diabetes, or
who have metabolic syndrome or glu-
cose intolerance (13–18). Although
cross-sectional studies have shown
that LBP levels are associated with an-
thropometric and metabolic measure-
ments (11,15,18), few longitudinal studies have investigated LBP in relation
to obesity- and diabetes-related mea-
sures (13). To our best knowledge, no
longitudinal studies have been con-
ducted among African ancestry men, a
population group disproportionally af-
fected by type 2 diabetes (19,20), and
thus, in particular, there is need for
such study. In the current study, we
tested whether baseline LBP is associ-
ated with changes in overall, central,
and skeletal muscle adiposity, glucose
homeostasis, and new cases of predia-
betes and type 2 diabetes in a cohort of
middle-aged and elderly African ancestry
men.

RESEARCH DESIGN AND METHODS

Study Population

Between 1997 and 2003, 3,170 previ-
ously unscreened men were recruited
for a population-based prostate cancer
screening study on the Caribbean island
of Tobago, Trinidad and Tobago (21). To
be eligible, men had to be ambulatory,
noninstitutionalized, and not terminally
ill. Recruitment for the survey was ac-
complished by flyers, public service an-
nouncements, and posters, informing
health care workers at local hospital
and health centers, and word of mouth.

Approximately 60% of all age-eligible
men on the island participated, and par-
ticipation was similar across the island
parishes. All men were invited to partic-
ipate in a follow-up clinic examination
between 2004 and 2007, and 2,031
men (70% of survivors) and 451 new
participants completed the visit. Men
were invited to complete a dual-energy
X-ray absorptiometry (DXA) whole-body
scan and a peripheral quantitative com-
puted tomography (pQCT) scan of the
lower leg. This visit represented the
baseline for the current study. Between
2010 and 2013, we invited these men to
return for repeat clinical examinations
and DXA and pQCT scans. The baseline
and follow-up visits followed the same
procedures for questionnaire inter-
views, biospecimen collection, and DXA
and pQCT scans. A total of 1,611 men
completed the follow-up assessment
(82% of survivors). On the basis of power
calculations (see STATISTICAL ANALYSES be-
low), we randomly selected 580 of these
men for the current study of LBP. The
Institutional Review Boards of the Uni-
versity of Pittsburgh and the Tobago
Ministry of Health and Social Services
approved this study. All participants pro-
vided written informed consent before
data collection.

pQCT Scan

A pQCT scan of the calf was performed
using the Stratec XCT-2000 to evaluate
skeletal muscle fat and muscle cross-
sectional areas. Scans were obtained at
66% of the calf length, proximal to the
terminal end of the calf. This site was
chosen because it is the region of the
lower leg with the largest circumference

with very little variability across in-
dividuals (22). Different tissues in the
analyses were separated according to
different density thresholds, using the
“soft tissue” algorithm. On the basis of
this calibration, fat, muscle, and cortical
bone are measured with mineral equiv-
alent densities of 0, 80, and 1,200 mg/cm³,
respectively. Therefore, changes in mus-
cle tissue to fat-like tissue will be de-
tected as a shift in mineral equivalent
density of the muscle from 80 to 0 mg/cm³.

Images of the cross-sectional area of
skeletal muscle and fat were analyzed
using Stratec 5.5D analysis software
(Orthometrix, Inc., White Plains, NY).

To maintain consistency, all images were
analyzed by a single investigator. We
assessed intramuscular fat using mea-
sures of calf muscle density (mg/cm³).

Muscle density is a valid measure of
fat accumulation within the skeletal
muscle and reflects the fat content
such that greater intramuscular fat is
associated with lower muscle density
(23).

DXA Absorptiometry Measures

DXA measurement of total body and
trunk fat was made using a Hologic QDR
4500 W densitometer (Hologic Inc., Bedford, MA). Scans were analyzed with
QDR 8.26a software.

Anthropometric Measurements

Standing height was measured to the
nearest 0.1 cm using a wall-mounted stadiometer. Body weight was re-
corded to the nearest 0.1 kg without shoes on a
balance beam scale. BMI was calculated
from body weight and standing height
(kg/m²). Waist circumference was mea-
sured at the narrowest point of the
waist using an inelastic fiberglass tape.

If there was no narrowest point, waist
circumference was measured at the
umbilicus.

Inflammation and Metabolic Variables

All biochemical assays in fasting serum
samples were performed in the Heinz
Nutrition Laboratory at the University
of Pittsburgh. Fasting serum glucose
was measured using an enzymatic pro-
cedure; the coefficient of variation per-
centage (CV%) between runs was 1.8%.
Insulin was measured using a radioim-
munoassay procedure developed by
Linco Research, Inc.; the CV% between
runs was 2.1%. The degree of insulin re-
sistance (IR) was estimated by HOMA
according to the method described by


Matthews et al. (24). In previous studies, HOMA-IR has correlated reasonably well with insulin clamp techniques (25). Baseline fasting serum LBP was measured using a Human LBP ELISA kit (Cell Sciences, Canton, MA) according to the manufacturer’s protocol. Manufacturer reported inter- and intra-assay CV% were 9.8–17.8% and 6.1%, respectively.

Other Measures
Information on lifestyle habits (current smoking [yes/no], walking more than twice in the past week [yes/no], watching 14 or more hours of television per week [yes/no], and current intake of alcohol of more than 3 drinks per week [yes/no]), history of medical conditions, and medication use were assessed using standardized interviewer-administered questionnaires. Men were asked to bring all prescription medications taken in the past 30 days to their clinic visit. Participants also rated their overall health status compared with men their own age. Type 2 diabetes was defined as currently taking an antidiabetic medication, regardless of fasting serum glucose level, or having a fasting serum glucose of ≥126 mg/dL. Impaired fasting glucose (IFG), also known as prediabetes, was defined as a fasting serum glucose level of 100–125 mg/dL. Low HDL-cholesterol (HDL-c) was defined as a fasting serum HDL-c <40 mg/dL.

Statistical Analyses
We estimated that to have the power to detect a univariate correlation of 0.12 (β = 0.8, α = 0.05) between LBP and changes in adiposity or glucose homeostasis, we needed to assay at least 500 samples. Owing to assay requirements and formatting, we measured LBP in a final number of 580 men. We then categorized baseline serum LBP into quartiles (n = 145 each) and tested its association with baseline cross-sectional and longitudinal changes in metabolic measures using a test of linear trend. Cross-sectional models were first adjusted for baseline age and then were additionally adjusted for smoking, walking, history of cancer, perceived health status, and alcohol intake. Longitudinal models were first adjusted for baseline age and baseline metabolic measures and then additionally adjusted for smoking, walking, history of cancer, perceived health status, alcohol intake, and low HDL-c status. We used multivariable logistic regression to test for an association of LBP with new cases of IFG or type 2 diabetes identified at follow-up. Models for IFG were run in only those with normal glucose at baseline, whereas models for type 2 diabetes were run in individuals without diabetes at baseline only. Odds ratios were expressed per 1-SD greater serum LBP. Statistical significance was based on an α = 0.05, and analyses were performed using SAS 9.3 software (SAS Institute, Inc., Cary, NC).

RESULTS
General Baseline Characteristics
Baseline characteristics for the 580 African ancestry men overall and according to quartiles of LBP are reported in Table 1. The men were an average ± SD age of 59.1 ± 10.5 years. Only 8% of men were current smokers, 9% had moderate alcohol intake, 38% watched more than 14 h of television in a week, and 88% typically walked for exercise. Approximately 5% of men had a history of cancer, and 6% had a history of any cardiovascular disease. Prevalence of IFG, type 2 diabetes, high triglycerides, low HDL-c, and hypertension were high, at 23%, 21%, 19%, 22%, and 53%, respectively. Greater LBP quartile was associated with greater baseline age, having diabetes, low HDL-c status, and taking antidiabetic medication (P < 0.05 for all). However, having a history of cancer decreased with increasing quartiles of LBP (P = 0.04).

Association of LBP with Adiposity and Metabolic Measurements at Baseline and Follow-up
Average follow-up time was 6.0 years (range 4.6–8.5). Greater baseline LBP was associated with greater baseline BMI, waist circumference, whole-body and trunk fat percentage, and fasting insulin, and HOMA-IR and inversely associated with skeletal muscle density independent of age and other covariates including smoking, walking, history of cancer, health status, alcohol intake, and low HDL-c status (all P < 0.05) (Table 2).

Baseline LBP was associated with an increase in trunk fat (P = 0.025) and HOMA-IR (P = 0.034) at follow-up after adjustment for all significant covariates (Table 3). LBP was also associated with a decrease in calf skeletal muscle density in minimally adjusted models (P = 0.048) (Table 3). However, the association was attenuated after additional adjustment for smoking, walking, history of cancer, health status, alcohol intake, and low HDL-c status (P = 0.057).

Associations of LBP with New Cases of IFG and Type 2 Diabetes
At the follow-up visit, 13.5% of normoglycemic men from baseline had developed IFG and 8.2% of men free of diabetes at baseline had developed type 2 diabetes (Table 4). Baseline LBP levels were positively associated with new cases of IFG, independent of age, trunk fat percentage, physical activity, health status, and low HDL-c status. Each 1-SD greater baseline LBP was associated with an ~51% increased risk of IFG (95% CI 1.02–2.21). The association was slightly attenuated and of borderline significance after accounting for change in trunk fat (P = 0.067), BMI (P = 0.046), or skeletal muscle density (P = 0.052). Baseline LBP was not significantly associated with new cases of diabetes.

CONCLUSIONS
To our knowledge, our study is the first to examine LBP and longitudinal changes in adiposity, glucose homeostasis, and diabetes risk in a population of African ancestry men, who have a high risk of developing type 2 diabetes. We found that greater LBP levels are associated with increasing central and skeletal muscle adiposity and IR as well as with an increased risk for developing IFG. Adjusting for changes in adiposity attenuated the association between LBP and IFG, suggesting that increased adiposity may play a causal role in the LBP association. These data provide further evidence for a potential link between LBP and age-associated increases in adiposity and impaired glucose metabolism.

Chronic inflammation is believed to be a risk factor for obesity and IR (26,27). LPS is derived from the outer membrane of gram-negative bacteria (4,5), and although low levels of LPS can be found in the circulation of healthy individuals, higher levels can produce inflammatory responses (5). LBP is expressed at constitutively low
levels and increases in the presence of inflammatory cytokines such as IL-6 and IL-1 (5). LBP functions by binding to LPS, which accelerates LPS binding to CD14 and subsequent presentation to macrophage TLR4 receptors (7). Importantly, Cani et al. (28) showed that chronic infusion of LPS caused weight gain in mice similar to that of a high-fat diet, thereby linking metabolic LPS from the gut microbiome to systemic inflammation and weight gain.

### Table 1—General characteristics of 580 African ancestry men overall and by quartile of LBP

<table>
<thead>
<tr>
<th>Trait</th>
<th>Overall</th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBP (µg/mL)</td>
<td>22.3 (8.4)</td>
<td>12.6 (3.8–16.8)</td>
<td>19.2 (16.8–21.3)</td>
<td>23.9 (21.3–27.1)</td>
<td>33.4 (27.2–57.4)</td>
<td>N/A</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.1 (10.5)</td>
<td>57.2 (10.6)</td>
<td>59.5 (10.2)</td>
<td>59.2 (10.1)</td>
<td>60.4 (10.9)</td>
<td>0.0188</td>
</tr>
<tr>
<td>Lifestyle (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoking</td>
<td>7.6</td>
<td>4.9</td>
<td>10.3</td>
<td>6.2</td>
<td>8.3</td>
<td>0.5233</td>
</tr>
<tr>
<td>Watch ≥14 h television/week</td>
<td>37.8</td>
<td>37.5</td>
<td>38.2</td>
<td>41.7</td>
<td>34.3</td>
<td>0.7332</td>
</tr>
<tr>
<td>Walk ≥3×/week</td>
<td>87.6</td>
<td>88.9</td>
<td>91.7</td>
<td>85.5</td>
<td>84.0</td>
<td>0.0920</td>
</tr>
<tr>
<td>Drink ≥4 drinks/week</td>
<td>8.8</td>
<td>6.3</td>
<td>9.7</td>
<td>9.7</td>
<td>9.0</td>
<td>0.4272</td>
</tr>
<tr>
<td>Comorbidities (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any cancer</td>
<td>4.8</td>
<td>6.9</td>
<td>5.5</td>
<td>5.5</td>
<td>1.4</td>
<td>0.0408</td>
</tr>
<tr>
<td>Any cardiovascular disease</td>
<td>5.9</td>
<td>6.3</td>
<td>3.5</td>
<td>5.5</td>
<td>8.3</td>
<td>0.3435</td>
</tr>
<tr>
<td>Hypertension</td>
<td>52.6</td>
<td>46.5</td>
<td>54.5</td>
<td>57.2</td>
<td>52.1</td>
<td>0.2965</td>
</tr>
<tr>
<td>High triglycerides</td>
<td>19.0</td>
<td>17.9</td>
<td>16.1</td>
<td>20.0</td>
<td>22.3</td>
<td>0.2458</td>
</tr>
<tr>
<td>Low HDL-c</td>
<td>21.9</td>
<td>18.6</td>
<td>19.6</td>
<td>20.0</td>
<td>29.5</td>
<td>0.0343</td>
</tr>
<tr>
<td>Good/excellent health</td>
<td>93.1</td>
<td>93.4</td>
<td>95.9</td>
<td>93.1</td>
<td>89.5</td>
<td>0.1054</td>
</tr>
<tr>
<td>IFG</td>
<td>23.1</td>
<td>27.8</td>
<td>20.0</td>
<td>22.8</td>
<td>21.5</td>
<td>0.3087</td>
</tr>
<tr>
<td>Diabetes</td>
<td>20.9</td>
<td>18.8</td>
<td>15.9</td>
<td>20.0</td>
<td>29.2</td>
<td>0.0201</td>
</tr>
</tbody>
</table>

Values are presented as mean (range), mean (SD), or as indicated. N/A, not applicable. *P value was determined using a test for linear trend across quartiles of LBP.

### Table 2—Association of LBP with baseline anthropomorphic and metabolic measures in African ancestry men

<table>
<thead>
<tr>
<th>Anthropometric and metabolic measures</th>
<th>Overall Mean (SD)</th>
<th>12.6 (3.8–16.8)</th>
<th>19.2 (16.8–21.3)</th>
<th>23.9 (21.3–27.1)</th>
<th>33.4 (27.2–57.4)</th>
<th>P value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 (4.8)</td>
<td>25.5 (0.4)</td>
<td>25.5 (0.4)</td>
<td>26.3 (0.4)</td>
<td>27.3 (0.4)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>92.4 (10.8)</td>
<td>91.2 (0.9)</td>
<td>90.4 (0.9)</td>
<td>92.5 (0.9)</td>
<td>95.7 (0.9)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Whole-body fat (%)</td>
<td>20.5 (5.5)</td>
<td>19.6 (0.4)</td>
<td>19.7 (0.4)</td>
<td>20.5 (0.4)</td>
<td>22.3 (0.4)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Amount of whole-body fat in trunk (%)</td>
<td>48.6 (5.3)</td>
<td>48.2 (0.4)</td>
<td>47.5 (0.4)</td>
<td>49.3 (0.4)</td>
<td>49.6 (0.4)</td>
<td>0.0034</td>
</tr>
<tr>
<td>Calf muscle density (mg/cm³)</td>
<td>73.5 (4.3)</td>
<td>74.2 (0.3)</td>
<td>74.1 (0.3)</td>
<td>73.5 (0.3)</td>
<td>72.3 (0.3)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Glucose† (mg/dL)</td>
<td>92.2 (12.0)</td>
<td>92.4 (1.1)</td>
<td>91.5 (1.1)</td>
<td>91.4 (1.1)</td>
<td>93.7 (1.2)</td>
<td>0.5031</td>
</tr>
<tr>
<td>Insulin† (mg/dL)</td>
<td>12.2 (6.5)</td>
<td>11.0 (0.6)</td>
<td>11.8 (0.6)</td>
<td>12.6 (0.6)</td>
<td>13.7 (0.6)</td>
<td>0.0012</td>
</tr>
<tr>
<td>HOMA-IR†</td>
<td>2.8 (1.6)</td>
<td>2.5 (0.1)</td>
<td>2.7 (0.1)</td>
<td>2.9 (0.1)</td>
<td>3.1 (0.2)</td>
<td>0.0017</td>
</tr>
</tbody>
</table>

Baseline values are presented as mean (SE). †Multivariable models include adjustment for baseline age, smoking, walking, history of cancer, health status, alcohol intake, and low HDL-c status. Lumbar microdysgenesis is reported only in men who were nondiabetic at baseline (n = 457).
LBP has been widely suggested to correlate with coefficients ≥0.6. In addition, LBP has been widely suggested to be a potential marker of gut-derived LPS and consequent LPS-induced inflammation (13,15,17,18). Therefore, most current human research infers that LBP variation is both correlated and caused by variation in LPS. However, it is also possible that variations in LBP in our study may be due to variations in cytokines or an acute-phase reaction unrelated to LPS (29).

Our findings that LBP was significantly and positively associated with baseline obesity measures are in line with other findings in the literature (11–13,16–18). A longitudinal study among 2,529 Chinese individuals found that higher baseline levels of LBP were correlated with an increased number of metabolic syndrome components (13). In contrast, baseline LBP measurements were not related to changes in BMI, waist circumference, whole-body fat, or fasting insulin levels in our sample. However, we found that LBP was associated with an increase in trunk fat over an average of 6 years’ follow-up. Our findings raise the possibility that LPS may be more strongly associated with central adiposity, which is a stronger risk factor for type 2 diabetes, than overall adiposity (30). An association of LBP with adiposity is biologically plausible because LBP, which is primarily produced by hepatocytes, is also produced by adipocytes in response to local proinflammatory cytokines (12).

Table 3—Association of baseline serum LBP with new cases of impaired fasting glucose and diabetes in African ancestry men

<table>
<thead>
<tr>
<th>Model</th>
<th>New cases of IFG in non-IFG subjects at baseline (N IFG/non-IFG: 43/275)</th>
<th>P value</th>
<th>New cases of diabetes in subjects without diabetes at baseline (N diabetic/ nondiabetic: 35/393)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age</td>
<td>1.50 (1.04–2.17)</td>
<td>0.0300</td>
<td>1.19 (0.81–1.73)</td>
<td>0.3753</td>
</tr>
<tr>
<td>2. Age + walking + health status + low HDL-c status</td>
<td>1.52 (1.03–2.22)</td>
<td>0.0332</td>
<td>1.22 (0.83–1.79)</td>
<td>0.3234</td>
</tr>
<tr>
<td>3. Model 2 + trunk fat</td>
<td>1.51 (1.02–2.21)</td>
<td>0.0376</td>
<td>1.16 (0.79–1.70)</td>
<td>0.4620</td>
</tr>
<tr>
<td>4. Model 3 + change in trunk fat</td>
<td>1.44 (0.98–2.12)</td>
<td>0.0668</td>
<td>1.16 (0.79–1.71)</td>
<td>0.4514</td>
</tr>
</tbody>
</table>

Odds ratios (95% CIs) are shown for 1-SD greater LBP.
without diabetes and positively associated with insulin at baseline, although this association was not confirmed by changes in insulin during follow-up. One previous study found that higher levels of serum LBP correlate with HOMA-IR (17), while another found that an association with HOMA-IR may depend on obesity status (16).

We also found, for the first time, that greater LBP levels are associated with a lower skeletal muscle density and its decrease with aging, indicative of an increase in ectopic skeletal muscle adiposity. This finding is in line with other previous data, in particular, a study using mouse models, which showed that LPS injections can lead to changes in muscle quality (31). Ectopic skeletal muscle adiposity is greater among African ancestry individuals than Caucasians (32–36) and has been shown to be an important risk factor for type 2 diabetes (37,38). Whether LBP may partly explain ethnic/racial differences in skeletal muscle adiposity is unclear. Our findings will need to be confirmed in other populations, including those of African ancestry.

In our sample, greater LBP was associated with an increase in IR and increased odds of newly generating an IFG over 6 years of follow-up. However, LBP was not significantly associated with new cases of type 2 diabetes. TLR4 activation on insulin target cells by LPS can lead to activation of the Jun N-terminal kinase and inhibitor of κB kinase pathways, both of which can inhibit insulin’s action by blocking phosphorylation of insulin receptor substrates proteins and increasing insulin receptor substrates degradation. Furthermore, the Jun N-terminal kinase/inhibitor of κB kinase pathways lead to activation of nuclear factor-κB, which increases production of proinflammatory cytokines and further inhibits insulin signaling (1). Skeletal muscle TLR4 expression is known to be higher in individuals who are obese or who have type 2 diabetes and to correlate with IR (39). LBP is a marker of circulating LPS and facilitates the binding of LPS to TLR4; thus, LBP may be an important biomarker for predicting the development of IR due to LPS-induced inflammation, and therefore, prediabetes. Lack of a significant association with new cases of type 2 diabetes in our population may be due to lack of statistical power, although a recent publication by Zhou et al. (40) suggests that LBP measurements alone are not sufficient to predict type 2 diabetes. Alternately, LBP may be an important marker of only the early metabolic disturbances seen in prediabetes. Future studies are needed to more definitively test this hypothesis.

A strength of our study lies in its longitudinal design. Only one other longitudinal study has been conducted to date, and it was in a Chinese population (13). In addition, the availability of DXA and CT measures allowed us to more accurately describe general and regional body fat distribution associated with LBP, compared with previous studies.

Our study also has some limitations. Our sample included middle-aged and elderly African ancestry men, and thus, our findings may not apply to younger men, women, or other ethnic groups. Also, dietary data were limited in our study and because dietary influences can affect gut bacteria or may affect diabetes risk through other means, having information on food intake could allow for us to have a more holistic picture of how lifestyle might affect LBP. We currently do not have liver function or disease information for our sample. LBP is primarily a hepatically produced protein, and the liver is a site for ectopic fat development; thus, this information may be an important factor to investigate in future studies. Finally, we measured LBP only at baseline and, therefore, cannot examine whether change in LBP is a stronger correlate of metabolic changes than a single LBP measurement.

In conclusion, the current study shows that greater serum LBP concentrations are associated with increases in trunk and skeletal muscle adiposity and IR with aging among African ancestry men. The association with IFG and early changes in IR suggest that LBP may be more informative among individuals with normal serum glucose. Further research is needed to better understand the mechanisms underlying the relationship between LBP, adiposity, and IR and prediabetes.

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