A “Gender Blind” Relationship of Lean Body Mass and Blood Pressure in the Tecumseh Study

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**Background:** Body size correlates positively with blood pressure (BP) but there is controversy about the roles of obesity versus muscularity in this relationship.

**Methods:** We examined the BP relationship with overweight, lean body mass (LBM), and muscle performance in 231 adolescents (17.25 ± 3.07 years, 123 males). The skinfold thickness (SKINT) was used to measure overweight, as this was a growing population.

**Results:** Maximal foot torque, a measure of muscle strength, correlated strongly (r = 0.51, P < .001) to LBM attesting to the validity of the calculated LBM. Anthropometric measurements were available also in 944 adults (29.9 ± 5.5 years, 461 men). Correlations of LBM to systolic (adolescents r = 0.52, adults r = 0.19, both P < .001) and diastolic (adolescents r = 0.47, adults r = 0.20, both P < .001) BP were highly significant. SKINT also correlated significantly to systolic and diastolic BP in adolescents and in adults, respectively. In both genders and populations an increasing SKINT was associated with a similar increase in BP, but this effect was superimposed on an average 10 mm Hg between-gender BP difference. The LBM in both groups and genders related to the BP in an identical fashion; the men were on the high and the women on the low end of the same BP/LBM correlation line. Thus, the amount of LBM erased categoric BP differences between the genders.

**Conclusions:** The gender-related BP differences appear to reflect the inherent gender differences in muscle bulk. Am J Hypertens 2002;15:258–263 © 2002 American Journal of Hypertension, Ltd.

**Key Words:** Blood pressure, gender differences, lean body mass, overweight dual-energy x-ray absorbiometry.
adults gave us an opportunity to reexamine this relationship. We confirmed that the lean body mass is an important correlate of systolic and diastolic BP in these populations and we suggest that this interesting relationship deserves further mechanistic studies.

**Methods**

**Adolescents**

The Tecumseh offspring study investigated 251 young subjects, most of whom (90%) were children of previous Tecumseh study participants. The present report is based on 231 (123 males) adolescents and teenagers (average age, 17.25 ± 3.07 years) in whom complete data sets are available. University of Michigan Institutional Review Committee approved this study. After signing written informed consent with their parents, the children were examined during the morning in the field clinic in Tecumseh. All participants were instructed not to eat after the previous evening’s dinner. The examination consisted of anthropometric measurements and of determination of the maximal muscle torque.

Because the age and body build varied we used a pediatric BP cuff in smaller subjects. If the bladder of the pediatric cuff did not encompass 75% of the forearm circumference, an adult cuff was used. The sitting BP was measured in a quiet room 5 min after the cuff had been placed on the right forearm. Three measurements taken 1 min apart were averaged and entered into the database.

The muscle performance was assessed in the recumbent position. A subject’s dominant foot was strapped to a hinged plate and another strap was placed just above the knee to immobilize the leg. The upper edge of the foot strap was at the first and fifth distal metatarsal bones. The positions of the sphygmonanometer and strap were measured. The plate was bolted to a single axis transducer (model FD 2-2000, Advanced Medical Technologies Inc., Newton, MA) and the data were recorded in a computer running Lab. VIEW software. The digital data were passed through a 10-tap low-pass filter with a stop frequency of 20 Hz. Several points along the curve were then analyzed for maximum strap force generated and maximum change in strap force/time. The strap force was converted to torque about the ankle using the sphygrion-strap position length.

Skinfold thickness (SKINT) was measured by calipers at the biceps, triceps, subscapular, and suprailiac region. The LBM was calculated by 1959 the Metropolitan Life formulas as:

\[
\text{Males} = \text{Weight} - \frac{[\text{Sum of skinfold} \times 0.26078 + 5.2745]}{100} \times \text{Weight}
\]

and

\[
\text{Females} = \text{Weight} - \frac{[\text{Sum of skinfold} \times 0.2654 + 13.081]}{100} \times \text{Weight}
\]

**Results**

**Findings in Adolescent–Teenager Population**

The general characteristics of the primary study population are given in Table 1. There was a slight preponderance of male subjects in the study and the Table shows the anticipated gender differences in BP and body size. The gender and age adjusted interrelation of variables of interest are given in Table 2. In this study of a population with various degrees of physical growth, we used SKINT as the

<p>| Table 1. Adolescents baseline data | Male ((n = 123)) | Female ((n = 108)) |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
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<p>| Table 2. Adolescents combined age and gender adjusted Pearson correlations |
|-------------------|------------------|------------------|------------------|------------------|------------------|</p>
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<th>Ave DBP</th>
<th>Skinfold</th>
<th>LBM</th>
<th>Height</th>
<th>Weight</th>
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<td>0.26‡</td>
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<td>0.19‡</td>
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</tbody>
</table>

Abbreviations as in Table 1.  
* \(P < .05\); † \(P < .01\); ‡ \(P < .001\).
reliable index of overweight. The BP strongly correlated with LBM and SKINT. The correlation of the BP with height was considerably weaker.

We also measured in this population the maximal foot torque as an index of muscle performance. The maximal torque was strongly correlated with LBM, height, and BP, but the correlation with SKINT was weak. A graphic illustration of these interrelationships for the whole population is given in Fig. 1. The strength of various relationships, adjusted for gender and age, is represented by the thickness of the line. The figure shows that systolic and diastolic BP strongly correlated to both the LBM and the SKINT. The LBM and SKINT were also related ($r = 0.47, P < .001$).

**Analysis By Gender of the Relationships of Anthropometric Measurements to the BP**

**Adolescents** The correlations between anthropometric measures and BP were similarly strong in both genders. However, the expected gender differences in BP, LBM, and SKINT (Table 1) suggested that a separate analysis of these relationships in each gender might be in order. The SKINT correlated with the BP in both genders, but the relationship in men was shifted 10 mm toward higher pressure levels. The slope of the relationship was the same in both genders. The correlation equation was Systolic BP = 105 + 0.75 × Average SKINT for males and Systolic BP = 95 + 0.75 × Average SKINT for females. The LBM, however, related to the BP in the same fashion in both genders and the equation was Systolic BP = 84.4 + 0.51 × LBM.

These relationships have been examined by multiple stepwise linear fitting. Three statistical models have been tested: 1) the relationship for males and females is colinear, 2) the two lines are parallel, and 3) two intersecting lines may describe the observation. The model of two parallel lines best described the relationship of BP to SKINT in both genders. The slopes were parallel but the intercept in men was 10 mm Hg higher. When the relationship of the BP and LBM was examined the model of parallel lines was rejected. It was, however, possible to fit one line for both genders.

Similar data have been obtained also for diastolic BP but are not shown in detail.

**Adults** The findings in adolescents in this study prompted us to investigate whether similar relationships could be found in adult Tecumseh study participants.

Akin to young individuals, a strong correlation of
SKINT with the BP was seen also in adults, $r = 0.25$ for systolic BP and $r = 0.26$ for diastolic BP (both $P < .001$), adjusted for age and sex, respectively. The curves for men and women were parallel, but in men the relationship was shifted to higher BP values. The correlation equations were Systolic BP $= 112 + 0.42 \times$ Average SKINT for males and for females $101 + 0.42 \times$ Average SKINT. The statistical model found two parallel lines and rejected colinearity. The between-gender BP difference was similar as at younger age (11 mm Hg in adults v 10 mm Hg in the young), but the slope of the effect of SKINT in adults was less steep (0.42 in adults v 0.75 in the young). Similar to observations in the younger group, the relationship between the LBM and BP also erased the gender BP differences among adults. The equation describing that relationship is Systolic BP $= 91.7 + 0.43 \times$ Age-adjusted LBM.

Combined Young and Adult Populations  The relationship of overweight (SKINT) and lean body mass to systolic BP was evaluated also in the combined population of young and adult. This is illustrated in Fig. 2. In the figure the data for LBM and SKINT in both genders were divided into sixtiles, averaged, and given as single points. This permits a visual identification of trends by gender. However, the lines drawn in the figure were calculated from all individual points across the entire range of variables.

Fig. 2 delineates a fundamental relationship between the lean body mass and BP, which exists in both age groups, is equal in both genders, and erases the categoric BP differences between the genders.

Most of the adolescents in this study were offspring of original participants in the Tecumseh BP Study. Consequently some correlation between adolescents and adults reported in this study could have reflected morphometric similarities across two related generations. We repeated all analyses excluding the parents of our adolescents from the adult group. When all analyses were repeated with the remaining 769 unrelated adults from the original Tecumseh study, practically identical results were obtained. For example, the relationship of LBM to systolic BP is described by the term Systolic BP $= 89.5 + 0.45 \times$ LBM and the reanalysis finds Systolic BP $= 89.0 + 0.46 \times$ LBM. All the correlations retained the previous high statistical significance.

Discussion  Relationship of LBM to BP

The literature is not unanimous on the relationship of LBM to BP and on its importance. A few studies, includ-
ing a total of 337 subjects of whom 106 were female, are clearly negative.\textsuperscript{1,2} The strongest support for the relationship between LBM and BP comes from pediatric literature. A significant correlation was found by calculation of LBM\textsuperscript{3} and by DEXA absorbimetry.\textsuperscript{4} A total of 3579 subjects (of whom about 50% were male) were examined in these studies.

Studies of relatively lean populations in Korea, Africa, the Caribbean, and Nigeria\textsuperscript{5–7} support the notion that LBM may have an important relationship with BP. However, in two of these studies a threshold has been found below which the BMI in lean subjects does not further correlate with the BP (<21 kg/m\textsuperscript{2}). A total of 34,388 subjects participated in these studies.

In populations that are not lean, a correlation of indexes of overweight and LBM with BP is invariably found.\textsuperscript{8–10} However, the interpretation varies from the emphasis on LBM\textsuperscript{9,10} to commenting on LBM as an incidental finding of questionable significance.\textsuperscript{8} A total of 704 subjects have been investigated in these studies and simple correlation coefficients of LBM with systolic BP in both genders ranged from 0.34 to 0.60 and the diastolic from 0.36 to 0.50. In the present study the age- and gender-adjusted correlation of LBM was 0.52 for systolic and 0.47 for diastolic BP.

The effect of overweight in our study is superimposed on the gender-related BP difference. However, we believe that the relationship of LBM with BP is a fundamental one, as it is the same in women and men and it prevails in the youth as well as in adulthood. Women and some lean teenagers fall on the lower portion of the same LBM–BP function line, which, at the higher end, is occupied by men and by some highly muscular women. Therefore, the gender difference in BP appears to reflect gender differences in LBM.

Methodologic Considerations

In our study we used the SKINT to assess LBM. Lean body mass assessed by underwater weighing correlates very well with LBM calculated from skinfold measurements.\textsuperscript{13,14} The correlation coefficient ranged from 0.71 to 0.82. In the present study, akin to the study by Viitasalo et al.\textsuperscript{10} the muscle strength strongly correlates with LBM. This provides external validity to the calculated LBM, as most of LBM comes from skeletal muscles and individuals with larger muscle mass ought to have stronger muscle performance.

The Nature of the “Gender-Blinded” Relationship Between LBM and BP: An Agenda for Research

Muscle Pressor Reflexes The skeletal muscle is a source of potent BP elevating reflexes. Isometric exercise,\textsuperscript{15} muscle stretching during orthopedic procedures,\textsuperscript{16} and external compression of skeletal muscles,\textsuperscript{17,18} elicit a large BP elevation, which in the presence of a prolonged stimulus may be sustained over long periods of time.\textsuperscript{16,19} However, the magnitude of these BP increases depends only on the muscle tone developed during isometric work and not on the size of the muscle group. It is, nevertheless, possible that a larger body mass (lean and total) requires more muscle tone to support the larger frame. Because in mammals the body size is not related to BP, this relationship, if it exists, ought to be associated with upright posture. Investigating the relationship of LBM to BP levels and BP changes during sleep may provide a simple test of this hypothesis. Such data may be available to some investigators and the question deserves exploration.

Muscle Composition Alternatively, it is possible that composition of the skeletal muscle relates to BP levels. In a study of hypertensive (n = 22) and normotensive (n = 19) subjects, Juhlin-Dannfelt et al.\textsuperscript{20} found a negative correlation between the BP and the percentage of well-capillarized muscles. This suggested that the type of skeletal muscle fibers may be a hemodynamic determinant of BP. However, in the study of Daniels et al.,\textsuperscript{2} LBM positively correlated with BP, but the total peripheral resistance correlated negatively with LBM. We confirmed in the present study the finding of Viitasalo et al.\textsuperscript{10} that LBM and increased muscle strength are correlated with higher BP levels. These findings do not support the hypothesis of Juhlin-Dannfelt et al.\textsuperscript{20}; in addition to muscle size, the muscle torque generally positively correlates with the proportion of well-capillarized slow twitch fibers.\textsuperscript{21} Considerable biopsy, muscle performance, and BP data on normotensive subjects have been collected in Scandinavian countries. A reanalysis of such data as to the relationship of the LBM, muscle performance, and BP might be helpful.

Growth Factors The most plausible explanation of the relationship of LBM and BP is that they both reflect physical growth. In mammals, the BP increases steeply from birth until the attainment of full growth. Thereafter, BP increases less steeply and not uniformly. During maturation, the gain in LBM may be only a marker of growth, or alternatively, the skeletal muscle growth could be physiologically involved in the development of the higher BP.

Weder and Schork\textsuperscript{22} proposed a model of how growth may affect BP through renal mechanism. In their opinion the increase of the BP supports renal homeostatic mechanisms, which are needed to match the renal function to growth. Within that construct, the muscle growth would be only a marker of an underlying, essentially renal, increase of BP.

Alternatively, it is possible that a factor that stimulates skeletal muscle growth also accelerates smooth muscle growth. A growth-related thicker muscle layer of the arteriolar wall might, by Folkow’s mechanism,\textsuperscript{23} potentiate vasoconstriction and BP elevation. A possible corroboration of this hypothesis can be found in the close relationship between LBM and left ventricular mass (LVM).\textsuperscript{4,24–26} A total of 9055 subjects were involved in these studies. Interestingly, when the effect of body size was accounted
for, in two large epidemiologic studies, a negative correlation of SKINT with LVM emerged. The association of LBM with LVM does not necessarily prove the hypothesis of “parallel” growth. It is equally possible that the cardiac size reflects the increased cardiac work needed to serve a larger body. A larger body size is associated with increased blood volume and a higher cardiac output. Because, in all articles quoted, the BP contributed little to LVM, the stroke work and the heart rate appear to be the most important variables. The hypothesis of parallel growth of skeletal and smooth muscles could be indirectly tested. The hypothesis would gain support if the LBM remains related to LVM after the effect of average stroke work was considered. Furthermore, the hypothesis would be supported if the wall/lumen ratio of arteries (from biopsies) or minimal forearm vascular resistance (with plethysmography) were to correlate positively with LBM.

Other Issues Besides the mechanistic issues discussed, the strong correlation of LBM with BP and the apparent additive effect of overweight lend themselves to exploration of other interesting questions. We are inviting investigators who have access to large data sets to engage in such analyses.

Is there evidence for a “physiologic” relationship of LBM to BP as opposed to a “pathologic” relationship with overweight? Does LBM predict cardiovascular events, and if yes, is this BP dependent? Is there a “good” and “bad” BP elevation? In the ultimate line such an analysis may provide a new pathophysiologic framework to revisit the Pickering-Plat discussion as to whether hypertension in the general population is unimodaly or bimodally distributed.

Another interesting question is whether LBM predicts future overweight. Lean body mass and various indices of overweight are interrelated. Gain of weight continues throughout a subject’s life, whereas skeletal muscle growth levels off. Is it possible that some growth factor initially affects the muscle size and later the growth of fat mass? In colloquial terms, if a person cannot grow any more vertically, does he continue to grow horizontally?

In summary, the strong relationship of LBM with BP raises a number of interesting questions that can be further investigated.

References