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<td>Author(s)</td>
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Intra-abdominal fat accumulation is a hypertension risk factor in young adulthood
A cross-sectional study

Atsushi Takeoka, PhD, Jun Tayama, PhD, Hironori Yamasaki, MD, Masakazu Kobayashi, MD, Sayaka Ogawa, Tatsuo Saigo, Hiroaki Kawano, MD, Norio Abiru, MD, Masaki Hayashida, MD, Takahiro Maeda, MD, Susumu Shirabe, MD

Abstract
Accumulation of intra-abdominal fat is related to hypertension. Despite this, a relationship between hypertension and intra-abdominal fat in young adulthood is not clear. In this study, we verify whether intra-abdominal fat accumulation increases a hypertension risk in young adult subjects.

In a cross-sectional study, intra-abdominal fat area was measured using a dual bioelectrical impedance analysis instrument in 679 university students (20.3 ± 0.7 years, 425 men). Blood pressure and anthropometric factors were measured. Lifestyle variables including smoking, drinking, physical activity, and eating behavior were assessed with questionnaire. High blood pressure risk (systolic blood pressure ≥130 mm Hg and/or diastolic blood pressure ≥85 mm Hg) with increasing intra-abdominal fat area was evaluated.

Participants were divided into 5 groups according to their intra-abdominal fat area (<24.9, 25–49.9, 50–74.9, 75–99.9, and ≥100 cm2). As compared with the values of the smallest intra-abdominal fat area group, the crude and lifestyle-adjusted odds ratios (ORs) were elevated in larger intra-abdominal fat area groups (OR 1.31, 95% confidence interval (CI) 0.66–2.60; OR 3.38, 95% CI 1.60–7.57; OR 7.71, 95% CI 2.75–22.22; OR 18.74, 95% CI 3.93–105.64, respectively). The risk increase was observed only in men.

Intra-abdominal fat accumulation is related to high blood pressure in men around 20 years of age. These results indicate the importance of evaluation and reduction of intra-abdominal fat to prevent hypertension.

Abbreviations: 95% CI = 95% confidence intervals, ACE = angiotensin-converting enzyme, BIA = bioelectrical impedance analysis, BP = blood pressure, CT = computed tomography, CC = correlation coefficient, DBP = diastolic blood pressure, IAF = intra-abdominal fat area, IFA = intra-abdominal fat, MRI = magnetic resonance imaging, OR = odds ratio, RAS = renin-angiotensin system, SFA = subcutaneous fat area, SBP = systolic blood pressure.

Keywords: body fat distribution, electric impedance, intra-abdominal fat, sex characteristics, young adult

1. Introduction
Hypertension is a major risk factor for cardiovascular diseases, and the main risk factor for hypertension is obesity. In a review from the Framingham Heart Study,[1] in which participants were prospectively followed for up to 44 years, it was estimated that excess body weight (including overweight and obesity) accounted for approximately 26% and 28% of hypertension cases in men and women, respectively, and for approximately 23% and 15% of coronary heart disease cases in men and women, respectively.

The mechanisms of hypertension seen with obesity are explained by hemodynamic alterations (eg, elevation in cardiac output and relatively elevated systemic vascular resistance) and abnormalities in lipid and glucose metabolism related to fat distribution.[2] In particular, the risk is greatest in patients with abdominal obesity. In several studies, intra-abdominal fat (IAF) accumulation is positively related to the increasing prevalence of hypertension.[3,4]

The standard methods to evaluate IAF area (IAFA) are computed tomography (CT) and magnetic resonance imaging (MRI).[5] However, because of the high cost and radiation exposure, these imaging studies are not always feasible. The dual bioelectrical impedance analysis (dual BIA) instrument was recently developed.[6] It can determine IFA by measuring truncal impedance and surface impedance at the abdomen separately, each of which reflects the truncal adiposity and the
subcutaneous adiposity, respectively. The dual BIA instrument is optimized for use in a wide range of human variation by analyzing the size of the effect that each parameter such as age and sex can have on the calculation outcomes utilizing information technology. The IAF measured with the dual BIA instrument has good correlation with CT-measured IAF.\textsuperscript{[7–9]} The prevalence of obesity increases mostly in young adulthood around 20 years of age.\textsuperscript{[10]} Once a person becomes obese, it is difficult to reduce and maintain the body weight.\textsuperscript{[11]} Therefore, this time period is important for intervention.\textsuperscript{[12]} The reduction of IAF is thought to be beneficial for preventing hypertension, but the relationship between high blood pressure (BP) and IAF in young adulthood is not clear. In this study, we verify whether IAF accumulation increases the risk of high BP in young adult Japanese subjects.

2. Methods

2.1. Study design and participants

This cross-sectional study included 1573 young adults (907 men and 666 women). All the participants were third-grade students of Nagasaki University. They underwent annual health checkups, including anthropometric measurements, a self-reporting lifestyle questionnaire, and BP measurement from April to June 2013. None of them took antihypertensive medication. Informed consent was obtained for undergoing IAFA measurement with the dual BIA instrument (Omron Dual scan HDS-2000; Omron, Kyoto, Japan). Then, 697 (423 men and 272 women) agreed to undergo abdominal fat composition measurement and the data were used for analysis (Fig. 1). Comparing 876 subjects who did not provide consent for participation, 697 participants were heavier and had higher body mass index (BMI) and waist circumference (WC) (body weight 56.8 ± 8.2 vs 60.0 ± 11.7 kg; P<0.0001; BMI 20.6 ± 1.9 vs 21.6 ± 3.3 kg/m²; P<0.0001; WC 73.2 ± 5.4 vs 76.2 ± 9.2 cm; P<0.0001).

2.2. Anthropometric measurements

Anthropometric measurements including height, body weight, and WCs were assessed. Each participant was asked to wear light clothing and no shoes during the measurements. Height and body weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, using an electronic scale with attached stadiometer (TANITA DC-250; Tanita Inc., Tokyo, Japan). WC was measured at the midpoint between the lower costal margin and the level of the anterior superior iliac crest using a nonelastic tape.

2.3. Blood pressure measurement

Blood pressure was measured serially with an electrical sphygmomanometer (DM-3000; Japan Precision Instruments Inc., Gunma, Japan). Participants were asked to rest quietly for over 5 minutes before BP measurement. The representative values were calculated as follows. BP measurements were performed twice with the participant in the sitting position. The measurement with lower systolic BP (SBP) was chosen as the representative value. In this study, “high BP” was defined as SBP ≥130 mm Hg and/or diastolic BP (DBP) ≥85 mm Hg.

2.4. Dual BIA method and instrumentation

The dual BIA instrument calculates the cross-sectional area of IAF at the level of the umbilicus based on the measurement of electrical potentials resulting from the application of small electrical currents in the 2 different body compartments. The principles of IAFA determination by the dual BIA instrument were described previously.\textsuperscript{[13,14]} Briefly, the dual BIA instrument consists of a bioelectric impedance component that measures truncal and surface impedance of the body, and a device that measures the physical size of the abdomen. The 2 sets of electrodes are for limb and truncal placement. The limb electrodes consist of 4 clip-on electrodes placed on the wrists and ankles. The truncal electrodes are 8 pairs of electrodes 6 cm apart longitudinally that are fixed to a belt in pairs, 1 each for front and back, and positioned at an equal distance. The belt is adjustable, allowing the electrodes to be centered on the mid-sagittal line at the level of the umbilicus in the supine position. The truncal impedance is measured by applying electrical currents between the upper and lower limb leads and reading the voltage from the electrodes around the abdominal circumference. The surface impedance is measured by applying and measuring the voltage from the abdominal circumference electrodes. Other details of the study method were described previously.\textsuperscript{[6,7,13,14]} Measurements were performed at the end of expiration phase in normal breathing because measurement is affected by breathing phase. To avoid the interference of hydration status on results, measurements were done at the fasting morning with minimum of drink.

2.5. Lifestyle assessment

We assessed participants’ smoking status, drinking status, physical activity, and eating behavior with a self-reporting questionnaire. Current smoker was defined as smoking more than 1 cigarette per day habitually. Current drinker was defined as drinking more than 1 alcohol drink per week habitually. Physical activity was determined by asking participants whether they belong to sports clubs and/or if they walk more than 30 minutes per day. Eating behaviors were assessed using the 30 questions of the 50 items on the Sakata Eating Behavior Questionnaire,\textsuperscript{[15,16]} which have been shown to reliably discriminate between obesity patients and healthy people. The 30 questions were classified into 7 categories: cognition of constitution (3 items), motivation for eating (3 items), substitute eating and drinking (6 items), feeling of satiety (5 items), eating style (3 items), meal contents (5 items), and eating rhythm abnormalities (5 items). The questionnaire was complet-
Table 1
Demographic data of high blood pressure and normotension groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>All participants (n = 697)</th>
<th>High blood pressure (n = 88)</th>
<th>Normotension (n = 609)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD (95% CI) n (%)</td>
<td>Mean ± SD (95% CI) n (%)</td>
<td>Mean ± SD (95% CI) n (%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>425 (60.98)</td>
<td>74 (84.09)</td>
<td>351 (56.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Women</td>
<td>272 (39.02)</td>
<td>14 (15.91)</td>
<td>258 (43.6)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>20.3 ± 0.7 (20.2–20.3)</td>
<td>20.5 ± 0.9 (20.3–20.7)</td>
<td>20.3 ± 0.6 (20.2–20.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>Height, cm</td>
<td>166.3 ± 8.6 (165.7–167.0)</td>
<td>170.8 ± 7.7 (169.2–172.5)</td>
<td>165.7 ± 8.6 (165–166.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>60.0 ± 11.7 (59.2–60.9)</td>
<td>72.1 ± 14.2 (69.1–75.1)</td>
<td>58.3 ± 10.2 (57.5–59.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>21.6 ± 3.34 (21.4–21.9)</td>
<td>24.6 ± 4.3 (23.7–25.5)</td>
<td>21.2 ± 2.9 (20.9–21.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>76.2 ± 9.2 (75.6–76.9)</td>
<td>84.1 ± 12.0 (81.5–86.6)</td>
<td>75.1 ± 8.1 (74.5–75.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>44 (6.31)</td>
<td>8 (9.09)</td>
<td>36 (5.91)</td>
<td>0.2354</td>
</tr>
<tr>
<td>No exercise habit, %</td>
<td>491 (70.44)</td>
<td>58 (65.91)</td>
<td>433 (71.1)</td>
<td>0.3197</td>
</tr>
<tr>
<td>Eating behavior (4-point Likert scale score)</td>
<td>66.7 ± 11.2 (65.9–67.6)</td>
<td>65.8 ± 11.8 (63.3–68.2)</td>
<td>66.9 ± 11.2 (66.0–67.8)</td>
<td>0.39</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>118.7 ± 11.3 (117.9–119.5)</td>
<td>137.3 ± 8.3 (135.5–139.1)</td>
<td>116.0 ± 8.9 (115.3–116.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>88.0 ± 8.5 (86.6–87.3)</td>
<td>76.9 ± 9.8 (74.8–79.0)</td>
<td>66.7 ± 7.4 (66.1–67.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IFA, cm²</td>
<td>38.5 ± 20.0 (37.0–40.0)</td>
<td>53.9 ± 29.8 (47.8–60.0)</td>
<td>36.3 ± 17.4 (34.9–37.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SFA, cm²</td>
<td>123.8 ± 71.2 (118.5–129.1)</td>
<td>176.2 ± 92.8 (156.5–195.8)</td>
<td>116.2 ± 64.2 (111.1–121.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VS ratio</td>
<td>0.35 ± 0.16 (0.34–0.36)</td>
<td>0.38 ± 0.13 (0.35–0.41)</td>
<td>0.35 ± 0.16 (0.34–0.36)</td>
<td>0.1018</td>
</tr>
</tbody>
</table>

*Current smoker* is defined as participants who smoke more than one cigarette per day habitually.
*Current drinker* is defined as participants who drink more than one alcohol drink per week habitually.
Eating behavior was assessed using the 30 questions of the 50 items on the Sakata Eating Behavior Questionnaire.
P values were calculated by the unpaired t test.

Table 2
Relationship between IFA and risk of high blood pressure in all participants.

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of persons with high blood pressure/no. of participants</th>
<th>Crude odds ratio (95% CI)</th>
<th>Adjusted for age, sex, smoking, drinking, exercise, and eating behavior (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFA, cm²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I1: ≤ 24</td>
<td>11/164</td>
<td>1.00 (reference value)</td>
<td>1.00 (reference value)</td>
</tr>
<tr>
<td>I2: 25–49</td>
<td>34/384</td>
<td>1.35 (0.69–2.86)</td>
<td>1.31 (0.66–2.80)</td>
</tr>
<tr>
<td>I3: 50–74</td>
<td>27/117</td>
<td>4.17 (2.02–9.15)</td>
<td>3.38 (1.60–7.57)</td>
</tr>
<tr>
<td>I4: 75–99</td>
<td>11/24</td>
<td>11.77 (4.31–33.03)</td>
<td>7.71 (2.75–22.22)</td>
</tr>
<tr>
<td>I5: ≥ 100</td>
<td>5/8</td>
<td>23.18 (5.06–125.86)</td>
<td>18.74 (3.93–105.64)</td>
</tr>
</tbody>
</table>

©=confidence interval, I1–5=participants were divided into 5 groups according to their IFA range, IFA=intraperitoneal fat area.
IAFA and subcutaneous fat area (SFA) in the high BP group were significantly larger than those in the normotensive group (53.9 ±28.8 vs 36.3 ±17.4 cm²; P<0.0001 and 176.2 ±92.8 vs 116.2 ±64.2 cm²; P<0.0001, respectively).

To evaluate the relationship between IAFA and high BP, the participants were divided into 5 groups according to their IAFA range. The CCs between IAFA and SBP or DBP were significantly larger than those in the normotensive group (rSBP=0.64–3.43; rDBP=1.56–9.06; P<0.0001; Table 2). The CCs between IAFA and SBP or DBP were significant in men (rSBP=0.64–3.43; rDBP=1.56–9.06; P<0.0001, respectively); however, in women, no significant correlations were found (rSBP=0.29, P=0.0001; rDBP=1.56–9.06; P=0.0001, respectively).

### 4. Discussion

In the present study, we hypothesized that IAF accumulation increases the risk of high BP. The results showed a significantly increased risk of high BP associated with IAF accumulation in men. This relationship was significant when comparing between groups whose IAFA was ≤100 cm². On the contrary, the relationship was not significant in women. Therefore, our hypothesis was partially proved in men. Most of the studies evaluating the relationship between IAF accumulation and risk of hypertension are focused on the middle-aged or the older population. To the best of our knowledge, this is the first study that evaluates the risk ratio of high BP according to IAF accumulation in young adults.

Several studies demonstrated the relationship between IAFA and hypertension. Hayashi et al.[3] followed up 300 Japanese Americans for about 10 years and reported that IAFA measured by CT at baseline was correlated with increased prevalence of hypertension in the follow-up period. The increased hypertension risk associated with IAFA was significant after adjusting for WC.

![Image](image-url)
or SFA. Similar results were observed in studies of Japanese subjects and other ethnic groups. The participants of these studies were middle-aged. Our findings showed the risk in young adulthood. One study of adolescents reported a positive relationship between MRI-measured IAF and BP in boys. Thus, IAF accumulation is associated with high BP at least since adolescence. Although the Japan Society for the Study of Obesity made a caution on overaccumulation of visceral fat as CT-measured IAF ≤100 cm² is an important period for making lifestyle changes. In industrialized countries, most of young adults about this age leave their families and begin to make their own decisions. The decisions include those related to eating behavior, physical activities, smoking, and drinking, among others. In fact, a large portion of the population becomes obese in these years.

A systematic review evaluated the relationship between weight change and BP difference in adults. The relationship found between weight and SBP difference was 1 kg:1 mm Hg. However, in obese subjects, it is difficult to reduce weight and maintain it because weight reduction induces increased appetite and decrease of energy expenditure. This phenomenon is caused by cross-talk between adipose tissue and the central nervous system with adipokines such as leptin and ghrelin. Thus, an effective weight-reduction program should take into account these mechanisms. Many studies have investigated the efficacy of intervention in obesity-related hypertension. However, few studies have evaluated changes in IAF. The reason for this is the difficulty to measure IAF. Although the gold standards for measuring IAF are CT or MRI, these are not suitable for frequent evaluation because of the costs and radiation exposure. In the present study, we used the dual scan. This device is noninvasive, relatively costless, and easy to manipulate. Therefore, this device facilitates the frequent evaluation of IAF. The precise evaluation of the relationship between IAF change and BP will add new knowledge about appropriate intervention.

This single-center cross-sectional study of Japanese young adults has mainly 4 limitations. First, because the sample size of female subjects was small, sex-stratified multiple logistic analysis (Table 3) failed to show the relationship between IAF and high BP clearly. We also compared the tertiles of IAF in women. After adjustment of age, smoking, exercise, and eating behavior, the risk of high BP was not different within the groups (using the value of the lower IAF tertile group as reference, ORs and 95% CIs of high BP of middle and higher tertile groups were OR 0.96, 95% CI 0.11–8.17 and OR 0.58, 95% CI 0.07–3.59, respectively). In addition, linear regression analysis showed no significant relationship between IAF and BP in women (Table 4). Second, although family history is an important factor of high BP, variables in this study do not include family history. However, in 561 of 697 participants, family histories were confirmed, and after adjusting for family history, the results were not different. Third, salt sensitivity is supposed to be involved in high BP with IAF accumulation. Therefore, the amount of salt intake can be a bias, but these data were not obtained in the present study. In general, young adults with normal renal function have sufficient sodium extraction abilities. None of the participants had a history of kidney disease or detectable proteinuria. Fourth, this is a cross-sectional study, and it cannot demonstrate a causal relationship. However, the present study results suggest that IAF accumulation is a critical risk factor for high BP and an important target for intervention. Further studies are needed to elucidate the relationship between IAF change and BP.

5. Conclusions

Young adulthood around 20 years of age is an important time period for preventing hypertension. This study revealed that IAF accumulation is related to high BP in Japanese men around 20 years of age. Furthermore, an increase in the risk of high BP was observed in subjects with IAF ≤100 cm². These results indicate
the importance of evaluation and reduction of IAF to prevent hypertension.

References


