Body Fat Distribution and Uterine Leiomyomas

Fumio Sato 1, Motoi Nishi 1, Ryuichi Kudo 2, and Hirotugu Miyake 1

Purpose: Investigation of the etiological relationship between body fat and uterine leiomyomas.

Settings: This was a case-control study. Percent body fat was measured bioelectrically with a body fat analyzer.

Subjects: In Sapporo City, Japan, 100 women with uterine leiomyomas (pathologically diagnosed) and 200 controls who were confirmed to have no uterine leiomyomas by clinical examination.

Results: Among the four types classified by BMI (over/under 24.0) and percent body fat (over/under 30%), the occult obesity type (BMI<24.0 and percent body fat >30%) had the highest risk. There were no patients of muscular type (BMI≥24.0 and percent body fat ≤30%). Women with more than 0.80 of waist-to-hip ratio were also at significantly higher risk.

Conclusions: Occult obesity and upper body fat distribution may lead to the development of uterine leiomyomas. J Epidemiol, 1998; 8: 176-180.

body fat distribution, uterine leiomyoma, body fat analyzer

Though uterine leiomyoma, which is one of the commonest benign tumors, is detected in 20-25% of women, few definite causes of it have been clarified. Recently several investigators reported the relation between obesity and this disease. Most of them used body weight and body mass index (BMI) as indicators of obesity. But the amount of body fat, the fundamental cause of obesity, and body fat distribution, which is reportedly found to be related to obesity-related several diseases, should be taken into account. Employing the amounts of fat measured bioelectrically, we conducted a case-control study with respect to the etiology of this disease in Sapporo City, Japan.

MATERIALS AND METHODS

Sapporo City (1.8 million inhabitants) is the capital of Hokkaido which is the northernmost island of Japan. Cases were 100 women who lived in Sapporo and underwent hysterectomy or myomectomy against uterine leiomyomas in Sapporo Medical University Hospital or its affiliated hospitals from September 1994 to October 1995 (a total of four hospitals). Diagnosis of uterine leiomyomas was confirmed pathologically. Their ages ranged from 29 to 54 years (median 45 years). All of them were premenopausal. They had no other gynecological diseases. Body length and weight, and waist and hip circumferences were measured by one of the authors before operation (F. Sato).

Controls were 200 women who lived in Sapporo and took part in a screening program for gynecological diseases which was conducted by the Hokkaido Cancer Society (located in Sapporo City) in the same period as that of the cases without any past history of endometrial cancer, ovarian cancer, breast cancer, uterine leiomyomas or other neoplasms, or endocrinological diseases. All of them were confirmed to have no uterine leiomyomas through gynecological examinations including pelvic examination and Papanicolaou smear test by a trained gynecologist. All of them were premenopausal. Their ages ranged from 30 to 54 years (median 45 years).
Body length and weight were measured by one of the authors (F. Sato). The waist and hip circumferences were measured by themselves. Eligible measurements of waist and hip circumferences were obtained from 96 cases and 164 controls. (The remaining subjects refused the measurement.) In this study we employed the waist-to-hip ratio, not absolute values of them, in order to eliminate the bias resulting from the self-measurement of the waist and hip circumferences in the control group. To ascertain the accuracy of self-measurement of anthropometric parameters, we examined the differences in values of waist, hip, arm and thigh circumferences in 41 women between self-measurement and investigator measurement in the preliminary study. The differences in values were about 1 cm on average, except for thigh circumference (Table 1). The difference 1 cm is negligible, however, when the ratio is used. For example, the ratio of 68.6 cm (mean waist circumference of the controls) and 91.0 cm (mean hip circumference of the controls) is 0.7538. That of 67.6 cm and 90.0 cm (smaller than respective values by 1 cm) is 0.7511.

Percent body fat of both cases and controls was measured with a body fat analyzer (TBF-51, TANITA Co. Ltd., Tokyo) employing electrical impedance. The body impedance was measured by putting the soles of the foot (after being cleaned by alcohol) on the two electric poles. On the same conditions cases (before operation) and controls were measured (e.g., time (from pm 2 to pm 4, after urination), clothes worn (only underwear)).

It is reported that there is a significant correlation between percent body fat measured by bioelectric impedance method and that measured directly in water, and that the impedance method has small measurement errors.

All the anthropometric measurements including percent body fat were done twice, and the average values were employed. Student's t-test and the chi-square test were employed for statistical analysis. The odds ratios and 95% confidence intervals (CI) were calculated and tested for linear trends by using the Mantel-Haenszel procedure and Mantel's extension method.

RESULTS

The mean total period of education of the cases was 12.6 years (SD, 1.4 years), and that of the controls was 12.7 years (SD, 1.2 years). There was no significant difference between both groups.

Percent body fat, waist circumference, hip circumference,

| Table 1 | Differences in measurement values between self- and investigator-measurements (mean ± SD). |
|--------|-------------------------------------------------------------------------------------------------|
| Measured by         | Difference on average(cm) | Correlation coefficient |
| Waist(cm) | 69.8 ± 6.8 | 68.7 ± 6.3 | 1.1 | 0.94* |
| Hip(cm)   | 91.4 ± 3.7 | 90.6 ± 3.7 | 0.8 | 0.82* |
| Arm(cm)   | 26.5 ± 2.3 | 25.8 ± 2.2 | 0.7 | 0.87* |
| Thigh(cm) | 45.6 ± 2.9 | 42.5 ± 3.1 | 3.1 | 0.33NS |

*P<0.01
NS: not significant (P>0.10)

| Table 2 | Anthropometric measurements of cases and controls (mean ± SD). |
|--------|-----------------------------------------------------------------|
| Measurements       | Cases               | Controls               |
| Body length (cm)   | 155.6 ± 5.5NS       | 154.7 ± 5.1           |
| Body weight (kg)   | 55.7 ± 7.5NS        | 55.2 ± 8.5            |
| BMI (kg/m²)        | 23.0 ± 2.7NS        | 23.1 ± 3.3            |
| Total body fat (kg)| 17.0 ± 5.1NS        | 16.0 ± 6.1            |
| Percent body fat (%)| 30.0 ± 5.4**       | 28.2 ± 5.8            |
| Waist circumference (cm)| 71.6 ± 6.5**  | 68.6 ± 7.3            |
| Hip circumference (cm)| 89.4 ± 5.6*       | 91.0 ± 5.3            |
| Waist-to-hip ratio | 0.80 ± 0.05**      | 0.75 ± 0.05           |

* P<0.05
** P<0.01
NS: not significant (P>0.10)
Table 3. Odds ratios of anthropometric factors.

| Factors       | Cases | Controls | Odds ratios (95% CI) |
|---------------|-------|----------|---------------------|
| BMI (kg/m²)   |       |          |                     |
| <20.0         | 12    | 23       | 1.0                 |
| 20.0-24.0     | 59    | 117      | 0.97 (0.45-2.08)    |
| 24.0-26.4     | 14    | 27       | 0.99 (0.38-2.57)    |
| 26.4≤         | 15    | 33       | 0.08 NS              |
| trend*        |       |          |                     |

| Percent body fat(%)       |       |          |                     |
| <25.0         | 17    | 62       | 1.0                 |
| 25.0-30.0     | 31    | 74       | 1.53 (0.77-3.02)    |
| 30.0-35.0     | 37    | 47       | 2.87 (1.44-5.71)    |
| 35.0≤         | 15    | 17       | 3.22 (1.34-7.74)    |
| trend*        |       |          | 12.2 **              |

| Waist-to-hip ratio       |       |          |                     |
| <0.75         | 15    | 84       | 1.0                 |
| 0.75-0.80     | 31    | 54       | 3.21 (1.59-6.51)    |
| 0.80-0.85     | 34    | 19       | 10.02 (4.57-21.98)  |
| 0.85≤         | 16    | 7        | 12.80 (4.50-36.37)  |
| trend*        |       |          | 46.4 **              |

* chi-square value
**P<0.01
NS: not significant (P>0.10)

and the waist-to-hip ratio showed significant differences between cases and controls. However, body height, weight and BMI showed no significant difference (Table 2). There were also significant differences between multipara cases and controls concerning waist-to-hip ratio (cases, 0.80±0.05, n=72; controls, 0.75±0.05, n=154, P<0.001) and percent body fat (cases, 30.3±5.7; controls, 28.2.7, P<0.01).

Percent body fat and waist-to-hip ratio showed a significant grade-associated relationship. However, BMI (classified depending on the criteria of the Japan Society for the Study of Obesity) did not show such relationship (Table 3).

We categorized subjects into 4 groups with regard to fat distribution based on percent body fat (over/under 30%) and BMI (over/under 24.0; the borderline BMI of overweight in Japanese people). Those with body fat over 30% and BMI under 24.0, designated as occult obesity type, showed the highest risk. There were no patients in the group of body fat under 30% and BMI over 24.0 designated as muscular type (Table 4). Women who had upper body fat distribution were at high risk, independent of percent body fat and BMI (Table 5).

There were no significant correlations between percent body fat and the weight of leiomyoma (r=0.07, P>0.10), and between the waist-to-hip ratio and the weight of leiomyoma (r=0.04, P>0.10). Between the waist-to-hip ratio and the number of parity, there were no significant correlation, either (r=0.04, P>0.10).

Table 4. Odds ratios by percent body fat and BMI (95%CI in parentheses).

| Percent body fat | BMI <24.0 | 24.0≤ |
|------------------|-----------|-------|
| <30.0            | 1.00      | 1.00  |
| 30.0≤            | 3.71 (1.81-7.63) | 1.56 (0.88-2.76) |

*0 case vs 12 controls

Table 5. Odds ratios by waist-to-hip ratio vs percent body fat and BMI (95%CI in parentheses).

| Waist-to-hip ratio | Body Fat | BMI <24.0 | 24.0≤ |
|--------------------|----------|-----------|-------|
| <0.80              |          | 1.00      | 6.25 (2.68-14.61) |
| 0.80≤              | 1.92 (0.95-3.88) | 7.76 (3.64-16.52) |

| BMI                | Body Fat | BMI <24.0 | 24.0≤ |
|--------------------|----------|-----------|-------|
| <24.0              | 1.00      | 7.12 (3.25-15.58) |
| 24.0≤              | 0.54 (0.21-1.39) | 3.78 (1.78-8.05) |
DISCUSSION

Since uterine leiomyomas are often asymptomatic, we employed controls who were confirmed to have no uterine leiomyomas through gynecological exams. Actually no other methods would give a surer confirmation than the present one, since we can not examine the controls pathologically.

Another reason for the employment of the waist-to-hip ratio is that fat distribution can not be estimated through body fat measurement by bioelectric impedance alone, and that upper body obesity is strongly associated with obesity-related diseases 13,14.

The present study showed that women with occult obesity or having upper body fat distribution were at high risk for uterine leiomyomas. Since such fat is often visceral 15, visceral obesity may be one of the risk factors. Fatty condition may not be a direct cause but a modifying factor which makes progression of occult leiomyomas to a size detected clinically, since there were no significant correlations between it and the weight of leiomyoma.

Various sex and non-sex steroids are said to be related to the development of leiomyoma 16. Fat tissue is the place in which extraglandular estrogenic processes take place 17. However, it is unlikely that estrogen deriving from fat tissue plays an important role in the development of this disease, since the present study showed that women with both high percent body fat (≥30%) and high BMI (≥24.0), i.e., those of simple obesity type, were not at significant risk. Moreover, increase in the waist-to-hip ratio does not depend on estrogenic action 18,19. The development of leiomyoma, therefore, does not seem to be due to a simple estrogenic effect.

A high waist-to-hip ratio (even with low BMI) is a risk factor for coronary heart diseases 20. As far as the etiology in respect to body fat is concerned, uterine leiomyomas are similar to coronary heart diseases. It was reported that being an ex-athlete is a low risk factor for benign uterine tumors 20. This result seems to be consistent with the present results showing that women of the muscular type were least at risk. Exercise should be useful for the prevention of both coronary heart diseases and uterine leiomyoma.

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