Fat measurement by CT in pre- and post-menopausal patients with breast cancer

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Purpose

1 Purpose

To assess the relationship between fat and breast cancer, we investigated the difference in the amount of fat between pre- and post-menopausal breast cancer patients by measuring the fat areas on CT images acquired at the navel's position. Currently, malignant tumors comprise the most common cause of death in Japan(1). In Japanese females, the incidence of breast cancer is increasing(1). Therefore, research for the prevention and early detection of breast cancer is important. Bray suggested that the development of breast, prostate, endometrial, colorectal, and gallbladder cancers depends on the relationship between obesity and hormones(2). According to a World Health Organization (WHO) report, colon, breast, endometrial, kidney, and esophageal cancers may be associated with obesity and exercise insufficiency(3). In addition, Miyoshi et al. reported that the incidence of breast cancer was high in obese patients among postmenopausal females, and that there was no correlation in premenopausal females(4). In Japan, the number of obese patients is reportedly increasing(5). In this study, we measured the fat area at the navel's position as a reference for fat measurement based on CT data(6) from pre- and postmenopausal patients with breast cancer to compare the fat level between the two groups.
Methods and Materials

2 Methods and Materials

2-1 Subjects

In this study, we employed PET-CT data obtained on detailed examination and diagnosis in the Gunma Prefectural Cancer Center between April 2008 and December 2009. In all patients with breast cancer, pretreatment data were employed. The subjects were 136 patients, consisting of 63 with breast cancer (21 pre- and 42 post-menopausal) and 73 with other disorders (31 pre- and 42 post-menopausal). The mean (± standard deviation) age of the subjects was 40.8 ± 7.8 years in premenopausal patients with breast cancer, 60.2 ± 7.0 years in postmenopausal patients with breast cancer, 46.7 ± 8.2 years in premenopausal patients with other disorders and 62.4 ± 4.1 years in postmenopausal patients with other disorders. The protocol of this study was approved by the Ethics Review Board of the Gunma Prefectural Cancer Center. CT scans were performed with a 16 multidetector row CT scanner (Biograph 16; SIEMENS). The scan parameters were as follows: tube voltage at 120 kV, tube current of 170 mA, slice thickness of 0.5 mm for scanning and reconstruction, reconstruction interval of 0.5 mm, gantry rotation time of 0.5 s.

In this study, "other disorders" refer to data obtained from patients other than breast cancer patients. In addition, data were randomly selected under the following conditions. Firstly, there was no bias toward the same disease, because the same disease may be characterized by a high or low fat level. Secondly, the mean age was not lower than that of breast cancer patients. In females, the fat level increases generally with age. Therefore, the mean age was matched to that of reference subjects. Thirdly, reliable information on menopause was obtained. Thus, patients with other disorders were randomly selected from PET-CT data meeting these conditions. In addition, we excluded patients with large tumors, those with passage disorder of the digestive tract, and those who underwent surgery from the extracted data, in order to avoid marked changes in the fat level.

We employed PET-CT data for the following reasons: an inquiry regarding physiology is made on PET-CT; it is possible to confirm the presence or absence of menopause, which is the theme of this study. The height and body weight were measured immediately before examination, facilitating the assessment of the body mass index (BMI). In addition, the Japanese Society of Obesity recommended fat measurement by CT in the expired-air mode. In our hospital, PET-CT is performed in the expired-air mode. For these reasons, PET-CT data were used.
2-2 Fat measurements and evaluation

For fat measurements, we employed Viewer software, to facilitate the measurement of CT values, include in workstation of a PET-CT device. CT values corresponding to fat ranged from -140 to -40 Hounsfield Units (H.U.). This was established based on the results of histogram analysis at the fat position on transverse CT images. The fat area was determined by counting the number of voxels with CT values for fat on a specific transverse image. Subsequently, to determine the visceral fat area, subcutaneous fat was manually separated from visceral fat, as shown in Fig. 1 on page 5 (black line). The black line was established by tracing the muscle immediately below the skin. The subcutaneous fat area was determined by subtracting the visceral fat area from the total fat area. As shown in Fig. 1 on page 5, visceral fat was defined as an area inside the black line, and subcutaneous fat as an area outside the black line. In this study, the sum of visceral and subcutaneous fat was regarded as the total fat level.

For evaluation, the following items were compared, and the significance was tested using Student's t-test, and the difference with P<0.05 was considered significant.

1. Comparison of the BMI between pre- and postmenopausal patients with breast cancer
2. Comparison of the fat area at the navel's position between pre- and postmenopausal patients with breast cancer
3. Comparison of the fat area at the navel's position between postmenopausal patients with breast cancer and those with other disorders
Images for this section:

**Fig. 0:** Separation of visceral fat and subcutaneous fat. The black line was established by tracing the muscle immediately below the skin.

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Results

3 Results

Initially, we compared the BMI for pre- and postmenopausal patients with breast cancer. The values in the former and the latter were 23.10±5.70 and 23.06±3.58, respectively. There was no significant difference (P=0.96).

Secondly, we compared the total, visceral, and subcutaneous fat areas at the navel's position between pre- and postmenopausal patients with breast cancer. The results are shown in Fig.1 on page 8. When comparing the total fat area, the P-value was 0.42. When comparing the subcutaneous fat area, it was 0.78. The mean values of the two parameters were higher in postmenopausal patients with breast cancer, although there were no significant differences. However, for comparison of the visceral fat area, the P-value was 0.03, as presented in Fig.2 on page 8. In postmenopausal patients with breast cancer, the visceral fat area was significantly larger than that in premenopausal patients with breast cancer.

Finally, to examine the influence of age-related fat accumulation, we compared the fat area between pre-/postmenopausal patients with breast cancer and "patients with other disorders" meeting the conditions described above (Section 2-1). Fig.3 on page 9 shows the results of comparison of the total, visceral, and subcutaneous fat areas at the navel's position between premenopausal patients with breast cancer and those with other disorders. There were no significant differences in the total, visceral, or subcutaneous fat areas between the two groups (P=0.99, 0.53, and 0.83, respectively). However, for postmenopausal patients with breast cancer, the total, visceral, and subcutaneous fat areas were significantly greater than in those with other disorders (P=0.03, 0.04, and 0.02, respectively), as shown in Fig.4 on page 10. As representative cases, the results of the comparison of the visceral fat area between postmenopausal patients with other disorders and breast cancer are presented in Fig.5 on page 11.

Thus, there was no difference in the fat area between premenopausal patients with breast cancer and those with other disorders, whereas the fat area in postmenopausal patients with breast cancer was larger than in those with other disorders. This suggests that, the influence of fat in postmenopausal patients with breast cancer is more marked than in premenopausal patients with breast cancer or postmenopausal patients with other disorders. It is known that breast cancer is closely associated with female hormones(7). Strong estrogen activity or the attenuation of progesterone actions increases the risk of breast cancer(8). In addition, the site of estrogen production differs between pre-
and postmenopausal women(9). Before menopause, estrogen is produced in the ovary. However, it is produced in the extraovarian region, primarily in adipose tissue, after menopause(9). In this tissue, estrogen is synthesized from cholesterol via aromatase in adipose cells(10). When adipose cells are abundant, estrogen production increases. Briefly, in this survey, the fat level was high in postmenopausal patients with breast cancer, suggesting the enhancement of estrogen activity.

In this study, there was no significant difference in the BMI, whereas fat measurements showed a significant difference; therefore, fat measurements may be useful. For the diagnosis of obesity, it is important to evaluate the fat distribution. Matsuzawa et al. assessed the visceral and subcutaneous fat levels by X-ray CT(11-13). Many studies indicated that visceral fat accumulation was closely involved in risk factors for arteriosclerosis(14,15), such as diabetes(16,17), abnormalities in lipid metabolism(16,17), and hypertension(18,19). In addition, Ogura et al. reported the relationship between cancer and the fat distribution(20). This study confirmed that, the fat level in postmenopausal patients with breast cancer was higher than in premenopausal patients with breast cancer or postmenopausal patients with other disorders. This suggests that fat accumulation after menopause increases the risk of breast cancer in females.
**Fig. 0:** Comparison of the total, visceral, and subcutaneous fat areas at the navel's position between pre- and postmenopausal patients with breast cancer.

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Fig. 0: Comparison of visceral fat areas at the navel's position between pre- and postmenopausal patients with breast cancer (P=0.03).

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**Fig. 0:** Comparison of the total, visceral, and subcutaneous fat areas at the navel's position between premenopausal patients with breast cancer and those with other disorders.

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<table>
<thead>
<tr>
<th>Fat Area</th>
<th>Postmenopausal patients with breast cancer</th>
<th>Postmenopausal patients with other disorders</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fat area (cm^2)</td>
<td>260.61±107.61</td>
<td>216.87±75.31</td>
<td>0.03</td>
</tr>
<tr>
<td>Visceral fat area (cm^2)</td>
<td>81.26±47.32</td>
<td>63.64±26.63</td>
<td>0.04</td>
</tr>
<tr>
<td>Subcutaneous fat area (cm^2)</td>
<td>186.90±76.05</td>
<td>149.39±61.95</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Fig. 0:** Comparison of the total, visceral, and subcutaneous fat areas at the navel's position between postmenopausal patients with breast cancer and those with other disorders.

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Fig. 0: Comparison of the visceral fat area at the navel's position between postmenopausal patients with other disorders and breast cancer (P=0.04).

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Conclusion

4 Conclusion

If fat measurements on CT would reveal fat accumulation in postmenopausal women, it may be an indication of a high-risk group for breast cancer. Therefore, fat measurements with CT images would be useful for assisting breast cancer screening. In the future, fat assessments may contribute to the development of preventive medicine.
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