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平成24年度～26年度　総合研究報告書

2

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Lymph node shape in computed tomography imaging as a predictor for axillary lymph node metastasis in patients with breast cancer

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Abstract. The aim of the present study was to evaluate whether preoperative computed tomography (CT) is a useful modality for the diagnosis of axillary lymph node metastasis. The axillary lymph node status was examined in patients with primary breast cancer who had undergone surgery. In total, 75 patients were analyzed with preoperative contrast CT images, following which the patients underwent an intraoperative sentinel lymph node biopsy to determine possible predictors of axillary lymph node metastasis. The lymph node shape was classified into three groups, which included fat-, clear-and obscure-types. Multivariate analysis revealed that clear-type lymph nodes in preoperative contrast CT imaging may be an independent predictor of lymph node metastasis (odds ratio, 15; P=0.003). Therefore, the results indicated that preoperative CT examination is useful to predict axillary lymph node metastasis.

Introduction

Axillary lymph node excision in breast cancer was previously the standard optimal surgical procedure for breast cancer. However, currently this procedure is not always essential since the status of axillary lymph node metastasis can be predicted by an intraoperative sentinel lymph node biopsy (SNB) (1). Despite this development, a number of institutions in Japan perform lymph node excision for cases demonstrated to be negative by intraoperative SNB. Thus, axillary lymph node dissection tends to be unnecessary, particularly in a number of patients with early stage breast cancer (2).

Axillary lymph node metastasis is a multifactorial event, and several clinicopathological factors have been reported as predictors of lymph node metastasis in breast cancer (3). However, since only a few methods exist for precisely predicting the axillary lymph node metastasis of an individual patient with breast cancer, a number of patients may not receive appropriate treatment for such metastasis.

The development of diagnostic imaging systems has facilitated the evaluation of axillary lymph node metastasis prior to surgery for breast cancer (4). Computed tomography (CT) is one of the representative modalities that can be used to evaluate the lymph node status, and is commonly used in hospitals due to its noninvasive and inexpensive characteristics. However, the number of studies investigating the clinical usefulness of CT in determining the axillary lymph node status is limited (5).

Therefore, the aim of the present retrospective study was to examine whether contrast CT imaging for the preoperative evaluation of the axillary lymph node status was a clinically useful modality.

Materials and methods

Patients. A total of 75 patients with primary breast cancer that had undergone surgical treatment at the First Department of Surgery of Sapporo Medical University (Sapporo, Japan) between 2009 and 2010 were recruited for the study. The clinical data from the Medical Records Department were retrospectively obtained. Written informed consent was required from all patients. All the patients were Japanese females that had been pathologically diagnosed with invasive ductal carcinoma without distant dissemination by whole body CT and bone scintigraphy. In this department, preoperative contrast CT is normally performed.

Data on clinical information were confirmed from the medical records of the patients and are shown in Table I. Tumor status was classified according to UCLA-integrated staging system classification with tumor, node and metastasis categories (6). The expression of the estrogen receptor or progesterone receptor was designated as positive when positive staining was observed and a total Allred score of ≥3 was achieved. Tumors that were immunohistochemically scored 2+ or 3+ and were fluorescence *in situ* hybridization-positive, were regarded as HER2-positive (7). Patients were classified into the following two groups: Group A consisted of patients

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Figure 1. CT images showing (A) fat-, (B) clear-and (C) obscure-type axillary lymph nodes. CT, computed tomography.

who had been diagnosed as negative by SNB, while group B comprised patients who had been diagnosed as axillary lymph node metastasis-positive.

Evaluation of axillary lymph nodes by preoperative contrast CT. Although the axillary lymph nodes were not palpable in any patient, enhanced whole body CT (Aquilion 64; Toshiba, Tokyo, Japan) with contrast was preoperatively performed since this is the standard procedure in Japan. A helical CT unit (64-slice CT system; Light Speed VCT vision; GE Healthcare, Milwaukee, WI, USA) was used for the evaluation of the axillary lymph nodes. The patients were in a supine position and raised their arms during the CT examination. CT images of the axillary lymph nodes were obtained as 2-mm slices through the axilla. The most caudally located enhanced lymph nodes were considered to be the sentinel lymph nodes. Lymph node size and shape were evaluated, as well as the Hounsfield units (HU) of the axillary lymph nodes in the CT images. The average of the region of interest (ROI) was used to evaluate the HU as a CT score. Lymph node shapes were classified into three groups, according to a previous study (8). Nodes with an internal fat concentration were classified as the fat-type (Fig. 1A), those with a size of ≥10 mm that appeared as rounded nodes without any internal fat were classified as the clear-type (Fig. 1B), while the nodes with unclear borders were classified as the obscure-type (Fig. 1C).

SNB. Prior to the initiation of surgery, 3-5 ml indigo carmine was injected into the peritumor, as well as subcutaneous and intradermal portions of the areola. Sentinel lymph nodes were located following massaging the expected area for 2-3 min. All the sentinel lymph nodes identified were sliced into 2-mm sections and stained with hematoxylin and eosin. A surgeon conducted the SNB, while a pathologist evaluated the specimens during the surgery. Finally, SNB specimens were embedded in paraffin and evaluated.

Statistical analysis. Analysis of the continuous variables, including age, tumor size, lymph node size and the CT score, was conducted with the t-test, whereas the χ^2 test was applied for the categorical variables (Table I). For the logistic regression analysis, odds ratios and 95% confidence intervals (CIs) were calculated following adjustment for age. All the statistical analyses and corresponding P-values were two-sided, and $P<0.05$ was considered to indicate a statistically significant difference. All statistical calculations were performed using JMP version 9.0 software (SAS Institute, Cary, NC, USA).

Table I. Clinical characteristics of the 75 patients with breast cancer.

Characteristics	Patients
Mean age, years (range)	
Total (n=75)	56 (35-84)
Pre-menopause (n=28)	54 (32-60)
Post-menopause (n=47)	60 (40-82)
pT[a], n (%)	
pTis	14 (18.7)
pT1	23 (30.6)
pT2	38 (50.7)
HR status, n (%)	
ER(+), PgR(+)	40 (53.4)
ER(+), PgR(-)	19 (25.3)
ER(-), PgR(+)	7 (9.3)
ER(-), PgR(-)	9 (12.0)
HER2 status, n (%)	
Positive	11 (14.7)
Negative	64 (85.3)
pN[a], n (%)	
pN0	56 (74.7)
pN1	19 (25.3)
pN2	0 (0)
Surgery, n (%)	
Breast-conserving	28 (37.3)
Mastectomy	47 (62.7)

[a]UCLA-integrated staging system classification with tumor, node and metastasis categories (2002). HR, hormone receptor; ER, estrogen receptor; PgR, progesterone receptor.

Results

Characteristics of the patients. A total of 75 patients who had received adequate treatment for primary breast cancer were