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Feasibility study of axillary reverse mapping for patients with clinically node-negative breast cancer

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Abstract

Background: The axillary reverse mapping (ARM) procedure was developed to identify and preserve arm lymphatic drainage during axillary lymph node dissection (ALND), thereby theoretically reducing the incidence of arm lymphedema. However, the oncological safety of this procedure has not yet been determined.

Methods: Two hundred ninety-two patients with clinically negative nodes (cN0) underwent both sentinel lymph node (SLN) biopsy and ARM. SLN was identified by dye and gamma probe methods, and ARM nodes were identified using a fluorescence imaging system. If SLN was histologically positive, ALND was performed with removal of ARM nodes. Otherwise, identified ARM nodes were preserved unless they coincided with SLN. Postoperatively, SLN as well as ARM nodes were histologically examined with H&E staining.

Results: SLN was identified in 286 of 292 patients, and ARM nodes were identified in 90 patients. In 54 patients with positive SLN, SLN was the same as the ARM node in 19 patients (the concordance type), whereas it was not an ARM node in the remaining 35 patients (the separate type). Non-SLN and ARM node was not involved in 51 of 54 patients with positive SLN, while it was involved in 3 patients of the concordance type.

Conclusions: When ARM nodes were involved in patients with cN0, these were most often the SLN-ARM nodes. Therefore, it may be concluded that ARM nodes that do not coincide with SLNs might be preserved during ALND in SLN-positive patients.

Keywords: Axillary reverse mapping; Sentinel lymph node biopsy; Fluorescence imaging; Breast cancer

Introduction

Axillary lymph node dissection (ALND) was the standard form of surgical management for breast cancer patients. However, this operation is associated with significant morbidity, the most functionally debilitating of which is arm lymphedema.[1] To reduce the incidence of lymphedema, sentinel lymph node (SLN) biopsy has been accepted to avoid unnecessary ALND in node-negative patients.[2,3] Nevertheless, node-positive patients who undergo ALND do not benefit from SLN biopsy. Moreover, SLN biopsy does not completely eliminate arm lymphedema. Recent short-term studies have demonstrated that lymphedema develops in 2–7% of patients with SLN biopsy alone.[4–6]

The axillary reverse mapping (ARM) procedure was developed to map and preserve arm lymphatic drainage to try to decrease rates of lymphedema in patients receiving

Abbreviations: ARM, axillary reverse mapping; ALND, axillary lymph node dissection; SLN, sentinel lymph node; H&E, hematoxylin–eosin; ICG, indocyanine green; SSM, skin-sparing mastectomy; NSM, nipple-sparing mastectomy.

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ALND and/or SLN biopsy.[7,8] This method is based on the hypothesis that there is separation of arm and breast lymphatic pathways, and the lymphatic pathway from the arm cannot be involved by metastasis of the primary breast cancer. Anatomically, however, there are lymphatic interconnections between lymph nodes draining the upper extremity and nodes draining the breast.[9,10] Although there was no involvement of ARM nodes in initial studies,[7,8] subsequent studies have shown that there are limits to the principle of non-overlap between breast and arm nodes, including: (a) the ARM nodes may be involved with metastatic foci in patients with extensive axillary lymph node metastases,[11–16] and (b) the SLN draining the breast may be the same as the ARM node draining the upper extremity.[13,15–18] Nevertheless, recent studies have suggested that it is oncologically safe to preserve ARM nodes and lymphatics for patients with clinically negative nodes (cN0).[15,18–20] In the present study, we evaluated 292 patients with cN0 who underwent SLN biopsy and ARM procedure, and examined whether the ARM procedure is oncologically feasible in patients with positive SLN.

Patients and methods

Patients

Between May 2009 and December 2014, a study was performed in breast cancer patients with cN0 who underwent SLN biopsy and the ARM procedure. Patients with clinically positive nodes (cN1) were excluded from the study. None of the patients underwent chemotherapy and/or hormone therapy before the surgery, but patients who underwent SLN biopsy and ARM procedure before chemotherapy were included. Patients with needle biopsy proven high-risk ductal carcinoma in situ (DCIS) were included. All enrolled patients provided written informed consent as approved by the Clinical Investigation and Ethics Committees of the Kanazawa Medical University Hospital.

SLN biopsy

The SLN biopsy technique has been described previously.[21] Briefly, 2 mCi of Tc-99m-phytate (Dai-ichi Radioisotope Laboratories Co. Ltd., Tokyo, Japan) was injected peritumorally approximately 18 h prior to the time of surgery. One hour after tracer injection, lymphoscintigraphy was performed to identify the number and the location of SLNs. Before surgical prep, 2 mL of 1% patent blue dye (CI 42045; Wako Pure Chemical Industries Ltd., Osaka, Japan) was injected subareolarly and the breast was massaged for 5 min. Through either mastectomy incision or small axillary incision, a handheld gamma probe (Tyco Healthcare, Norwalk, CT) was used to identify areas of increased radioactivity within the axilla. All blue-stained nodes and hot nodes were removed, and hot SLNs were defined as any nodes with a 10:1 ex vivo gamma probe ration of SLN to non-SLNs. Then, excised SLNs were sent for pathological examination on frozen sections.

ALND and ARM procedure

The ARM procedure has also been described previously.[15] Before surgical prep, 0.1 mL (0.25 mg) of indocyanine green (ICG) (Diagnogreen; Daiichi Pharmaceutical, Tokyo, Japan) was injected subdermally into the inner side of the wrist, while 2 mL (5 mg) of ICG was injected subdermally into the upper inner arm in the initial 2 patients. The injection site was massaged until fluorescent ARM lymphatics were observed in the upper inner arm (the average duration of massage: 10 min). During SLN biopsy, an invisible near-infrared fluorescence imaging system (PhotoDynamic Eye; Hamamatsu Photonics, Hamamatsu, Japan) was used to identify the ARM nodes and/or lymphatics. The ARM nodes and/or lymphatics receiving ICG appeared in the axilla as shining fluorescent spots and streams in the fluorescence images (Fig. 1). When SLN was histologically negative, the identified ARM nodes were preserved unless they were the same as the SLN. When SLN was positive, however, ALND was subsequently performed with removal of ARM nodes. The conventional ALND procedure was modified to preserve the fluorescent lymphatics coming from the arm, but all of the fluorescent ARM nodes were selectively excised and sent for pathological examination separately from the other dissected axillary nodes.

Mastectomy

Partial mastectomy, total mastectomy, skin-sparing mastectomy (SSM) or nipple-sparing mastectomy (NSM) with or without immediate breast reconstruction was performed, depending on the extent of cancer in the breast and the patient's choice. In our department, partial mastectomy, SSM and NSM were usually performed with the so-called "moving window" operation using a wound retractor.[22,23]

Pathological examination

Each SLN was serially sectioned at intervals of approximately 2 mm during surgery, and frozen sections were cut and histologically examined with hematoxylin and eosin (H&E) staining.[21] Postoperatively, the remaining frozen tissue was thawed, fixed in 10% formalin, and processed routinely for sectioning with H&E staining. On the other hand, ARM nodes were removed during surgery and postoperatively from ALND specimen, and sectioned at intervals of approximately 2 mm, fixed in 10% formalin, and processed routinely for sectioning with H&E staining. However, complete ALND specimens were bisected along the long axis, and one section from each node was subjected to H&E staining. SLNs and ARM nodes as well as