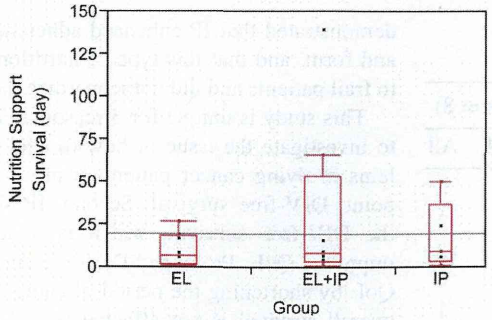


	Median (range)
EL arm	7 (1–27) days
EL+IP arm	8 (1–139) days
IP arm	9 (1–50) days

FIG. 4. Overall survival. EL = Ensure Liquid®; IP = Inner Power®.

Adverse Events

The incidences of adverse events are shown in Table 3. Nausea was seen more often in the EL arm (37.5%) than in the IP arm (0%) and EL + IP arm (12.5%).

QoL Score

The QoL scores based on EORTC QLQ-C15-PAL are shown in Fig. 6. There was a tendency toward better symptom scores in the IP arm with regard to fatigue and appetite loss. Specifically, the scores for fatigue were 94.5 in the EL arm, 75.5 in the EL + IP arm, and 75 in the IP arm, and the scores for appetite loss were 100 in the EL arm, 93.3 in the EL + IP arm, and 75 in the IP arm.

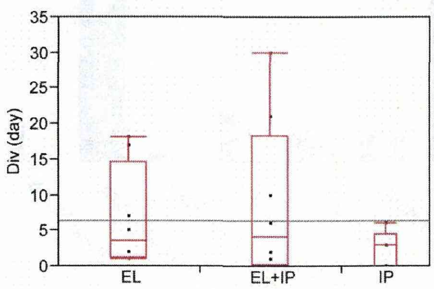
DISCUSSION

To the best of our knowledge, no other randomized trials have investigated the efficacy of nutritional support in end-of-life cancer patients. End-stage cancer patients suffer from a variety of symptoms. Emesis, anorexia, appetite loss, and vomiting are symptoms that are often seen, regardless of the primary sites. Parenteral hydration or tube feeding is often considered for such conditions (1). However, these procedures can be accompanied by pain and restriction of activities of daily living. The issue of whether ANH is necessary for end-of-life cancer patients remains questionable.

Recently, 2 Cochrane reviews were published concerning AH (21) and artificial nutrition in this setting (22). These reviews systematically searched for scientific evidence about ANH as an intervention and concluded that there were insufficient good quality studies to make any clinical recommendations.

Following these reviews, Bruera et al. reported the results of a RCT in 2013 (23). Their results revealed that 1 L of hydration per day for the last wk of a cancer patient's life conferred no benefit compared with placebo (100 ml of hydration per day) with regard to symptom scores arising from dehydration. The study also revealed that overall survival, which was 1 of the secondary endpoints, did not change despite hydration (21 days vs. 15 days). Although there was a limitation concerning low statistical power because of poor accrual, the merit of hydration in this setting was not shown.

Thus, there is no consensus about nutritional support for terminally ill cancer patients (7). Because it is difficult to precisely predict the prognosis of patients, the issues of when and how to start any nutritional support have always been problematic for clinicians. Although ANH is often used in the hospital setting, it is difficult to avoid worsening a patient's QoL. Furthermore, there are no established methods regarding the optimum amount, and calorie, protein, and fat contents (6,7). Thus, if a patient is able to intake anything orally, health workers should optimize the nutritional support by modifying the shape and taste of their diet, so the patient may continue to eat orally for as long as possible. Oral nutrition is most successful when there is an emphasis on "what one likes", rather than



	Median (range)
EL arm	3.5 (1–18) days
EL+IP arm	4.0 (0–30) days
IP arm	3.0 (0–6) days

FIG. 5. Duration of hydration. EL = Ensure Liquid®; IP = Inner Power®.

TABLE 3
Incidences of adverse events

	EL ($n = 8$)		EL + IP ($n = 8$)		IP ($n = 8$)	
	G 3/4	All	G 3/4	All	G 3/4	All
Anorexia	2	7	3	6	1	4
Nausea	3	4	1	1	0	3
Vomiting	0	1	0	0	0	0
Diarrhea	0	1	0	1	0	0
Constipation	0	1	0	2	0	1
Fatigue	0	4	0	4	0	4

EL = Ensure Liquid®; IP = Inner Power®.

"what is right or of value" nutritionally (24,25). However, there is a concern around this strategy. Questions that should be considered are "Is this way really the best for patients?" and "Could this approach shorten lives?" To investigate these matters, we set a composite endpoint of DIV-free survival. We considered that this endpoint can surrogate for QoL by showing a catheter-free period.

Providing an appropriate diet for dying patients is often difficult. Frail patients easily aspirate feeds and may develop fatal aspiration pneumonia (11). In addition, it is often difficult for these patients to eat foods that contain large amounts of fat, because high-fat foods can cause nausea and diarrhea and many patients do not like the taste of such products. IP is easily and safely consumed by patients because of its pudding-like form and nonfat "refreshing-beverage-like" taste. This is reflected in our results, because 70% of patients who used IP reported that the product tasted "good", whereas none of the patients who used EL answered in a similar fashion (data not shown). Because many of the patients liked the taste of IP, this may have led to the improved diet adherence. This trial has demonstrated that IP enhanced adherence because of its taste and form, and that this type of nutrition was safely delivered to frail patients and did not jeopardize their QoL or survival.

This study is unique for 3 reasons. First, it is the first RCT to investigate the issue of how to deal with nutritional problems in dying cancer patients using a novel composite endpoint, DIV-free survival. Second, IP significantly prolonged the DIV-free survival, which is a surrogate endpoint for improved QoL. Prolonged DIV-free survival means improved QoL by shortening the period of catheter use for hydration, if overall survival is not affected (Fig. 1). Third, we can conclude that oral nutritional support with IP did not appear to have any adverse effects on survival during the cancer patients' last days, because the overall survival periods in the IP and EL + IP arms were longer than that in the EL arm, although a statistical analysis was not performed.

LIMITATIONS

There are a couple of limitations to this study. This study was designed as a 3-arm exploratory trial, and the sample size was insufficient to draw definitive conclusions. In conducting this study, 6 of 27 patients (22%) dropped out. Although the attrition rate was not as high as that in a similar study (26), the present study's attrition rate made it difficult to conduct the research as planned. Because participant attrition can introduce bias when analyzing and reporting results, we will carefully monitor the patient status and avoid attrition for as long as possible when conducting further studies.

Although there appeared to be better QoL scores in the IP arm, the statistical significance was not analyzed. Besides, we could not collect sufficient QoL data during AH. To confirm that the composite endpoint of DIV-free survival can surrogate for QoL by showing a catheter-free period, it would be better

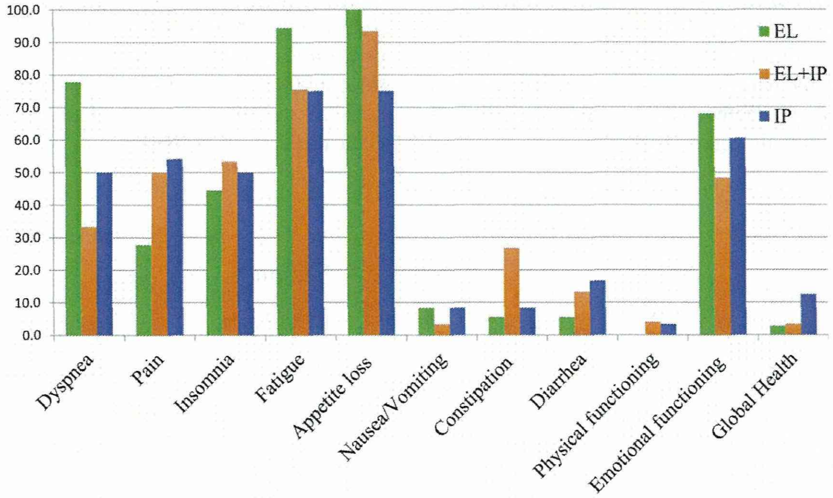


FIG. 6. EORTC-QLQ-C15-PAL and diarrhea scores. EL = Ensure Liquid®; IP = Inner Power®.

to collect QoL data both during nutritional support and after catheter introduction, and compare them in a future study.

CONCLUSIONS

We conducted this study to explore and investigate 3 hypotheses: 1) IP would prolong the duration of oral intake; 2) IP would shorten the duration of AH; and 3) IP would not affect survival rates.

The observed results in this trial indicate that these hypotheses were able to be confirmed. Therefore, a Phase III trial is warranted to show that IP can shorten the duration of parenteral hydration in terminally ill cancer patients and does not affect their survival.

FUNDING

This study was conducted as a joint study by The University of Tokyo and Otsuka Pharmaceutical Factory Inc. Financial resources and test agents were provided by Otsuka Pharmaceutical Factory Inc. The financial aid had no influence on the study outcomes and the authors were free to interpret the data according to a strict scientific rationale. There is no other conflict of interest to disclose.

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ORIGINAL ARTICLE

Omission of axillary lymph node dissection for clinically node negative early-stage breast cancer patients

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Received: 22 December 2013 / Accepted: 7 April 2014

Abstract
Background For clinically node negative (N0) breast cancer patients, sentinel node (SN) biopsy (SNB) is a standard technique and complete axillary lymph node dissection (ALND) remains the standard treatment when the SN is positive. However, the American College of Surgeons Oncology Group Z0011 trial and the International Breast Cancer Study Group 23-01 trial showed that SNB without ALND can offer excellent regional control and equal survival compared with ALND for limited macrometastatic and micrometastatic SN involvement, respectively. We retrospectively evaluated axillary control rates in clinically N0 patients who had no axillary surgical treatment.
Methods Data on 158 patients who underwent breast-conserving therapy without any axillary surgical procedure between 1994 and 2010 were extracted. The last follow-up was on May 2013, and the overall median follow-up period was 119.0 months.
Results Of all 158 patients, 10 (6.3 %) and 3 (1.9 %) developed locoregional and axillary recurrences, respectively. The 10-year locoregional and axillary recurrence rates were 5.8 and 2.1 %, respectively. The 5- and 10-year overall survival rates were 94.0 and 84.8 %, respectively. Cases with axillary recurrence tended to have common risk factors for recurrence.
Conclusion Even if SNB and ALND were omitted, local and regional recurrence rates were very low among clinically N0 patients and were at the same levels shown in recent trials. This suggests that at least ALND might be safely avoided in clinically N0 patients without any obvious risk factors regardless of axillary nodal status after SNB.

Keywords Axillary lymph node dissection · Breast cancer · Sentinel lymph node

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Introduction

The sentinel lymph node (SN) biopsy (SNB) has become established as the standard strategy for evaluating the axillary lymph node status in clinically node negative (N0) breast cancer patients [1–4]. According to guidelines of the American Society of Clinical Oncology (ASCO), complete axillary lymph node dissection (ALND) remains standard treatment for patients with axillary metastases identified by SNB. When SNB is performed under the direction of an experienced surgeon, patients with negative SNB results need not have complete ALND [1]. In Japan, this approach has been widely accepted and SNB became covered by health insurance in April 2010.

However, today, the role of ALND for clinically N0 patients has been questioned. Some prospective and retrospective studies have reported low axillary recurrence rates in patients with a positive SN who did not have complete ALND, especially in cases of micrometastases and isolated tumor cells (ITCs) [5–10]. Bilimoria et al. [5] reported that 20.8 % of women with SNB-proven positive SN underwent SNB alone and 79.2 % underwent SNB with complete ALND according to the National Cancer Data Base. In terms

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to collect QoL data both during nutritional support and after catheter introduction, and compare them in a future study.

CONCLUSIONS

We conducted this study to explore and investigate 3 hypotheses: 1) IP would prolong the duration of oral intake; 2) IP would shorten the duration of AH; and 3) IP would not affect survival rates.

The observed results in this trial indicate that these hypotheses were able to be confirmed. Therefore, a Phase III trial is warranted to show that IP can shorten the duration of parenteral hydration in terminally ill cancer patients and does not affect their survival.

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of morbidity, ALND might be unnecessary in the routine management of breast cancer in a setting of low risk of recurrence. Additionally, three large clinical trials, the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-32, the American College of Surgeons Oncology Group (ACOSOG) Z0011 and the International Breast Cancer Study Group (IBCSG) 23-01 trials have provided beneficial evidence regarding SNB. In the NSABP-B32, when the SN was negative, SN surgery alone without ALND was shown to be an appropriate, safe, and effective therapy for clinically N0 patients [11]. For SN-positive patients, the ACOSOG Z0011 trial showed that SNB without ALND could offer excellent regional control and did not result in inferior survival compared with performance of ALND in selected patients with early-stage breast cancer treated with breast-conserving therapy (BCT) and adjuvant systemic therapy [12, 13]. Findings from the IBCSG 23-01 trial are consistent with those of the ACOSOG Z0011 trial [14]. In this study, not performing ALND was not inferior to ALND in patients with one or more micrometastatic (≤2 mm) SNs and a tumor of a maximum of 5 cm.

In the present study, we retrospectively evaluated axillary recurrence rates in clinically N0 patients who in the past did not undergo any axillary surgical treatment (neither SNB nor ALND) for various reasons.

Materials and methods

Patients

From 1994 to 2010, more than 1,000 breast cancer patients received BCT at the University of Tokyo Hospital. In the current study, data on the patients who did not undergo any axillary surgical procedure (including SNB, sampling, or ALND) were extracted. Inclusion criteria were as follows: all patients had clinically Tis to T2 N0 M0 disease and received BCT without any axillary surgical procedure. Three patients with pT4 tumor with a little skin invasion were included because the entire growths had been removed safely. Excluded were patients who had synchronous bilateral breast cancers as were patients with a multicentric tumor. Therefore, 158 patients were eligible for the current analysis.

Although ALND was employed routinely in our institution at that time, most patients in this analysis rejected ALND due to ALND-associated morbidities, such as arm edema, impaired shoulder function and brachial plexus neuropathy. Also, some patients did not undergo ALND at a physician's discretion. After the SNB procedure was accepted in our institution, ALND has been frequently omitted for not-extended Tis disease.

The last follow-up was performed on May 2013. The 5- and 10-year patient follow-up rates were 91.6 and 57.5 %,

Table 1 Characteristics of patients and primary tumors

Characteristics	*n*	%
No. patient	158	
Age (year)		
Median	53	
Range	28–83	
Menopausal status		
Premenopausal (%)	59	37.3
Postmenopausal (%)	99	62.7
T stage		
Tis	26	16.5
T1	95	60.1
T2	32	20.3
T3	0	0.0
T4	3	1.9
Unknown	2	1.3
Receptor status		
ER+/PgR+	86	54.4
ER+/PgR−	29	18.4
ER−/PgR+	4	22.5
ER−/PgR−	29	18.4
Unknown	10	6.3
Estrogen receptor		
ER+	115	72.8
ER−	33	20.9
Unknown	10	6.3
Progesterone receptor		
PgR+	90	57.0
PgR−	58	36.7
Unknown	10	6.3
Her2 status		
Her2+	13	8.2
Her2−	59	37.3
Unknown	86	54.4
LVI		
Yes	55	34.8
No	97	61.4
Unknown	6	3.8
Grade		
1–2	110	69.6
3	10	6.3
Unknown	38	24.1
Surgical margin		
Negative	106	67.1
Positive	36	22.8
Dose	12	7.6
Unknown	4	2.5
Systemic chemotherapy		
Yes	39	24.7
No	119	75.3

Table 1 continued

Characteristics	*n*	%
Systemic hormone therapy		
Yes	94	59.5
No	64	40.5

respectively. At the analysis time, 21 (13.3 %) patients had died; 14 cause-specific deaths (8.9 %) and 7 deaths from other diseases (4.4 %). The overall median follow-up period was 119.0 months (range 14.7–215.4 months). Patient and tumor characteristics are shown in Table 1.

Treatment

All patients underwent lumpectomy. Histological type was classified according to World Health Organization criteria.

Then standard whole breast irradiation (WBI) was administered using a photon-beam energy of 6 MV by the tangential field technique to 50 Gy in 2.0-Gy fractions, 5 times weekly. An electron boost of 10 Gy in 5 fractions (range 10–14 Gy/5–7 fr) was delivered to the tumor bed depending on the margin status (both the positive and close surgical margins) at the site of excision and/or the presence of an extensive intraductal component. The borders of tangential fields were placed at the inferior border of the humeral head cranially, below the inframammary fold caudally, in the midline medially and in the midaxillary line laterally. No patient received specific irradiation to the axillary or supraclavicular lymph node area.

Adjuvant systemic therapy was determined at the discretion of the treating oncologist, considering risk factors, biological factors and patient preference. Some patients underwent neo-adjuvant chemotherapy.

Statistical analysis

Statistical analyses were performed using StatView Dataset File version 5.0J for Windows computers (Cary, NC, USA). Survival periods were defined as the time from breast surgery (or initial treatment) to either death or the last follow-up date. The recurrence-free survival (RFS) was the time to detection of the first relapse or the last follow-up date. Diagnosis of recurrence was based on physical, ultrasound, or radiographic examination, and few patients underwent biopsy of recurrent lesion. Survival curves and survival rates were estimated with the Kaplan–Meier method estimator. Acute toxicity was assessed and documented according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Late complications were graded in accordance with the National Cancer Institute Common Toxicity Criteria (NCI-CTC) Version 4.0.

Results

Locoregional recurrences

Of the 158 patients, 10 (6.3 %) developed locoregional recurrences after times of 20–134 months. In 4 patients, distant recurrences occurred simultaneously or subsequently. Axillary recurrences occurred in 3 (1.9 %) patients at 20, 53 and 65 months, respectively. Out of these 3 patients, 2 patients had an isolated axillary recurrence, whereas 1 had simultaneous axillary and local recurrences, and subsequently 2 patients developed distant metastases. The 10-year locoregional and axillary recurrence rates were 5.8 and 2.1 %, respectively (Fig. 1).

As shown in Table 2, a trend toward the following risk factors was suggested for axillary recurrence: young age, grade 3 tumor and Her2 disease. For locoregional recurrences, salvage mastectomy, chemotherapy, or hormonal therapy was performed.

As to distant recurrences, the 5- and 10-year distant recurrence rates were 7.4 and 12.0 %, respectively.

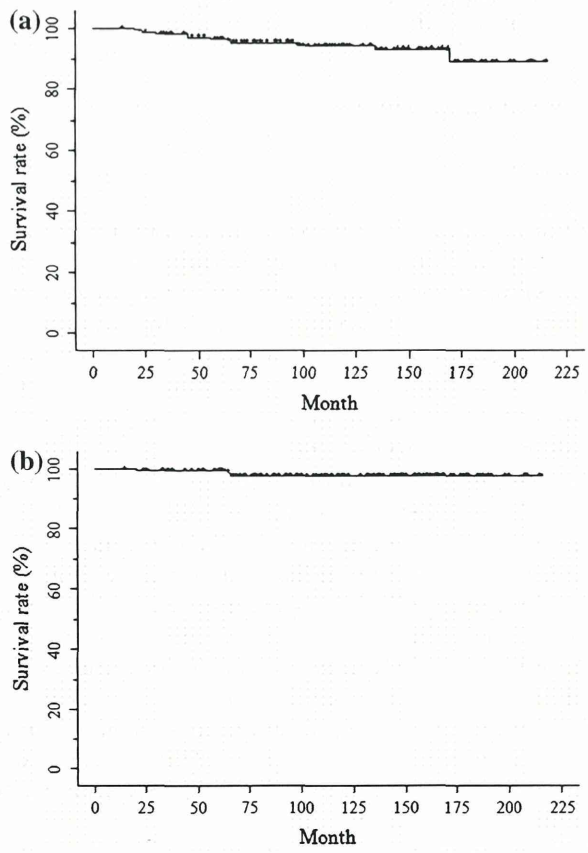

Fig. 1 Survival curve showing locoregional control rates (**a**) and axillary control rates (**b**)

Survival

The 5- and 10-year overall survival (OS) rates were 94.0 and 84.8 %, respectively (Fig. 2a). The 5- and 10-year cause-specific survival rates were 95.2 and 89.3 %, respectively. The 5- and 10-year RFS rates were 89.9 and 84.5 %, respectively (Fig. 2b).

Complications

In the acute phase, most of the patients experienced radiation dermatitis of Grade 1–2. Table 3 shows complications in the later phrase, with some patients experiencing Grade 2 or over toxicity. Two patients had arm edema (1, Grade 2; 1 Grade 3) and 3 had radiation pneumonitis (2, Grade 2; 1 Grade 3). There was no impaired shoulder function, no brachial plexus neuropathy and no pathologic fracture. Contralateral breast cancers occurred in 11 patients. No secondary cancer in the radiation field was observed; however, one patient developed acute lymphatic leukemia at 5 years and out of field cancers occurred in 13 patients.

Discussion

This single-institution retrospective study demonstrates that axillary recurrence rates in clinically N0 breast cancer patients who received BCT and did not undergo both SNB and ALND were low; the 5- and 10-year axillary

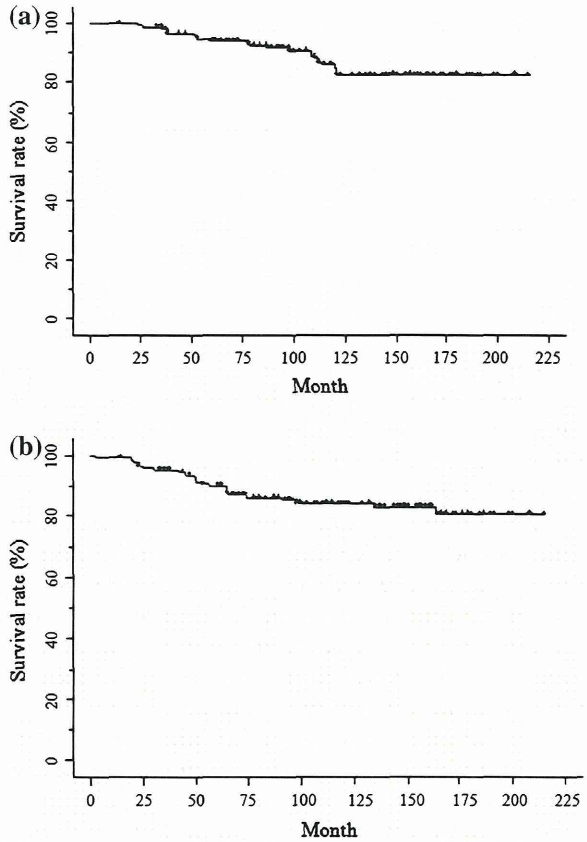

Fig. 2 Survival curve showing overall survival rates (**a**) and recurrence-free survival rates (**b**)

Table 2 Characteristics of patients with locoregional recurrence

Cases	Age	T stage	Surgical margin	HR	Her2	Grade	Adjuvant Tx	Locoregional recurrence			Distant metastasis	
								Period	Site	Therapy	Period	Site
1	*33*	*T1c*	–	–	*Unknown*	*3*	*CTx*	*5y3m*	*Ax*	*Unknown*	*5y3m*	*Hung, bong*
2	*63*	*T1b*	*+(DCIS)*	–	*+*	*1*	*NeoCTx*	*1y8m*	*Ax*	*ALND + trastuzumab*	*2y2m*	*Hung*
3	*36*	*T1s*	*+(DCIS)*	*+*	*Unknown*	*1*	–	*5y5m*	*Ax, Local*	*HT*	–	–
4	54	T2	Close	–	–	1	–	8y2m	Local	Tumorectomy	–	–
5	67	T2	–	+	Unknown	1	HT	11y2m	Local	Mastectomy	–	–
6	41	T1b	–	+	Unknown	2	–	3y9m	Local	Tumorectomy + HT	–	–
7	76	T1c	+	Unknown	Unknown	Unknown	HT	1y11m	Local	Mastectomy	3y	Brain
8	79	Tis	Close (DCIS)	+	Unknown	1	–	4y8m	Local	Tumorectomy + HT	–	–
9	51	T1c	–	–	–	Unknown	CTx	14y0m	Local	Tumocectony + HT	6y0m	Bone
10	76	Tis	–	+	–	1	–	2y6m	Local	Mastectomy	–	–

HR hormonal receptor, *DCIS* ductal carcinoma in situ, *Tx* therapy, *CTx* chemotherapy, *Neo CTx* neo-adjuvant chemotherapy, *HT* hormonal therapy, *Ax* axillary, *ALND* axillary lymph node dissection

Italicized are cases with axillary recurrence

Table 3 ≥ Grade 2 late complications

	No. of patients (%)			
	Grade			
	2	3	4	5
Arm edema	1 (0.6)	1 (0.6)	0	0
Pneumonitis	2 (1.3)	1 (0.6)	0	0

recurrence rates were 0.6 and 2.1 %, respectively. Similar analysis was reported by Sanuki et al. [15]. The 5-year cumulative incidences of axillary failure were 2.7 % for the 1,548 clinically N0 patients treated by BCT who did not receive both SNB and ALND, with the median follow-up period of 88 months.

Up to the present, most clinicians consider that women with SN metastases should undergo further ALND. In addition to its therapeutic implications, ALND also provides information about the status of nodal involvement. However, decisions on the systemic treatment modality are increasingly based on the intrinsic subtypes defined by clinico-pathological surrogate criteria rather than the risk of recurrence [16]. Furthermore, the need for ALND has been questioned and good axillary control in clinically N0 patients without ALND has been demonstrated.

In the ACOSOG Z0011 [12, 13], patients with one or two SN metastases detected by standard hematoxylin and eosin stain were randomized to undergo ALND after SNB versus SNB alone. There were no statistically significant differences in survival and locoregional recurrence between the two groups. The 5-year recurrence rates in the ipsilateral axilla were 0.9 % in the SNB alone group. Similarly, in the IBCSG 23-01 trial [14], patients with one or more micrometastatic SNs detected by SNB were randomly assigned to either undergo ALND or not undergo ALND. At a median follow-up of 5.0 years, there were no differences between the two groups in disease-free survival (DFS) and OS. Other reports also demonstrates that the proportion of patients who have SN metastases and did not undergo ALND have a lower risk profile for axillary recurrence [5–7], especially when SN involvement is micrometastatic or ITCs [8–10].

About SN-negative cases, the NSABP B-32 trial and the ACOSOG Z0010 trial show excellent regional control. In NSABP B-32 [11], women with invasive breast cancer were randomly assigned to either SNB plus ALND (group 1) or to SNB alone with ALND only if the SNs were positive (group 2). Among 3,986 SN-negative patients, 8-year OS rates and DFS rates were statistically equivalent between two groups, and regional recurrences as first events occurred in 0.4 % of group 1 and 0.7 % of group 2 ($p = 0.22$). The ACOSOG Z0010 [17], in which patients with negative SN were randomized to SNB alone and further ALND, found an axillary recurrence rates of 0.3 % in the SNB alone group.

All these studies about both SN-positive and negative cases imply that SNB and maybe adjuvant therapy also provide excellent regional control of clinical occult disease. Additionally, these recent studies and the current study suggest that at least ALND could be safely omitted in the context of BCT for patients with clinically N0 disease regardless of SNB results. Even though the SNB procedure is reported to have a false-negative rate of about 10 % [18] and about a half of patients with SN involvement is considered to have non-SN metastases [19], axillary recurrence rates are very low if SNB is employed appropriately [11, 15, 20].

One of the possible reasons for good control of the axilla is due to WBI. WBI may provide both treatment and preservation and contribute to achieving axillary control in clinically N0 patients. Although standard tangential irradiation is regarded to be insufficient to cover the entire axillary lymph node area, it seems to irradiate much of the level I area and part of the level II area. Standard tangential irradiation is used in many studies showing successful omission of ALND for patients with positive SN. Furthermore, the dose coverage in level I and II area is improved when the height of superior border of the standard tangential field is extended to the humeral head, i.e., using high tangential technique [21–25]. We apply high tangential technique routinely irrespective of the axillary surgical procedure.

One of the questions is whether high tangential technique is more effective than standard tangential technique, especially in cases of positive SN and no ALND. Although there are no definitive data comparing axillary outcome between these two techniques for this subgroup, high tangential irradiation might lead to excellent axillary control.

On the other hand, to cover the regional area as extensive as the dissected area by ALND, the three-field irradiation technique is applied in some studies [15, 26–28]. This technique has a separate anterior field that covers the supraclavicular fossa and axilla. Although Fujimoto et al. [26] demonstrated that three-field irradiation decreased the risk of regional recurrence in absolute terms compared with tangential irradiation only, the difference was small (4.8 vs. 2.4 % at 5 years; $p = 0.048$). Therefore, common or high tangential irradiation may be sufficient to control the regional area and the three-field technique is needed only for selected patients with higher risk.

Another possible explanation for the good axillary control is benefit from adjuvant therapy, especially chemotherapy. Although randomized control trial (RCT) from the Institute Curie showed superior locoregional control by ALND to axillary irradiation [29, 30], in that study, only a small portion of patients received adjuvant systemic therapy (chemotherapy, 19/326 in the ALND group and 9/332 in the radiation group; hormonal therapy, 14/326 in the ALND group and 8/332 in the radiation group). In contrast, 25 and 60 % of patients received chemotherapy and hormonal therapy, respectively, in this study. Nodal tumor deposits were found to be chemosensitive, and the adjuvant therapy resulted in the ablation of residual microscopic axillary metastases [31]. Appropriate systemic therapy appears to be beneficial for local and systemic control.

Risk factors for locoregional recurrence that have been recognized to date contain as follows: negative hormone receptor, large pathologic tumor size, high modified Bloom–Richardson score, young age, positive lymphovascular invasion and outer tumor location [12–14, 17]. In the current study, statistical analysis was not available due to the small study population. However, the 3 cases with axillary recurrence had the following features: younger age, estrogen and progesterone receptor negative, Her2 receptor positive and high grade. In fact, 2 of the 3 patients developed distant metastasis. Those patients with axillary recurrence seemed to have risk factors that coincided with those described in ACOSOG Z0011 [12, 13] and IBCSG 23–01 trial [14]. If SNB was performed to those patients, successive therapy and/or the outcome might have been a little different.

There are some limitations to this study. First, due to the nature of a retrospective study, there was a lack of information on biological factors and a lack of consistency of treatment including chemotherapy regimen, hormonal therapy duration and drugs. Second, despite the eligibility of T1–2 disease in the large clinical trials, small numbers of those with Tis (16.5 %) and T4 (1.9 %) disease were included in the analysis. However, their inclusion seemed to have an insignificant effect on the results.

Furthermore, current study and others showing no significant difference in patients with positive SN between ALND vs. no further ALND might raise doubts on the role of SNB itself. However, SNB is the standard approach for axillary staging at this time and it has some therapeutic role. Sanuki et al. [15] reported that SNB contributed to more accurate patient selection of patients who benefited from regional nodal irradiation and optimal systemic therapy instead of ALND. Ongoing studies are examining the omission of SNB in patients with ultrasound negative axilla, but this practice remains experimental [15, 32]. Patients with low risk factors such as hormone receptor positive, Her2 receptor negative, $\leq$T1 disease, grade 1–2 tumor and $\geq$50 years old can avoid SNB safely.

In conclusion, even if SNB and ALND were omitted, local and regional recurrence rates were very low among clinically N0 early-stage breast cancer patients at the same level as those shown by recent RCTs. This suggests that at least ALND might be safely avoided in those patients without any obvious risk factors regardless of axillary nodal status after SNB. WBI by standard or high tangential technique and systemic therapy based on intrinsic subtypes might have contribution to excellent axillary control, even if SN is positive. Although SNB seems not only to provide accurate staging information but also to have a therapeutic role, patients with low risk factors such as hormone receptor positive, Her2 receptor negative, $\leq$T1 disease, grade 1–2 tumor and $\geq$50 years old can avoid SNB safely. Further analysis will be necessary to accurately identify subgroups that can avoid SNB.

Conflict of interest None.

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