Clinical Study

Oncology

Oncology 2010;79:105–111
DOI: 10.1159/000320162

Received: May 7, 2010
Accepted after revision: July 20, 2010
Published online: November 22, 2010

Does the Metastatic Lymph Node Ratio Influence the Disease-Free Survival of Patients with Breast Cancer: Single-Center Experiences

Bala Basak Oven Ustaalioglu[a] Ahmet Bilici[a] Umut Kefeli[a] Mesut Şeker[a] Emre Yildirim[a] Taflan Salepci[a] Mustafa Oncel[b, c] Metin Kement[b] Mahmut Gumus[a]

Departments of [a]Medical Oncology, and [b]General Surgery, Dr. Lutfi Kirdar Kartal Education and Research Hospital Istanbul, and [c]Medical College of Gumushane University, Gumushane, Turkey

Key Words
Breast cancer · Lymph node ratio · Disease-free survival

Abstract
Background: Axillary lymph nodes (ALNs) are the most important prognostic factor for survival in breast cancer. Pathological evaluation can affect the number of involved lymph nodes. In the current study, we evaluated whether the metastatic lymph node ratio (n ratio) is important in predicting disease-free survival (DFS) for breast cancer patients. ***Material and Methods:*** From 802 breast cancer cases, 427 patients with ALN metastasis were analyzed retrospectively. The n ratio was categorized as n ratio 1 (1–10%), n ratio 2 (10.01–50%) and n ratio 3 (>50%). DFS was established according to the Kaplan-Meier method. Predicting risk factors for relapse were analyzed using the Cox proportional hazards model. ***Results:*** The n ratio was significantly higher in breast cancer patients with advanced pathologic pT, pN and clinical stage, undifferentiated histology, lymphovascular and extracapsular invasion, more resected ALNs and positive progesterone receptor. In the univariate analysis, multicentricity, necrosis, grade, pN stage, estrogen receptor and progesterone receptor positivity, trastuzumab and neoadjuvant chemotherapy usage, the presence of inflammatory breast cancer and n ratio were found to be important factors in predicting DFS. Multivariate analysis indicated that multicentricity, neoadjuvant chemotherapy, trastuzumab usage and n ratio were significantly associated with prognosis. ***Conclusions:*** The n ratio is inexpensive, easily available and a simple prognostic factor for breast cancer patients with positive ALNs.

Introduction

Breast cancer is the most common cancer in women and the second leading cause of cancer-related mortality in postmenopausal women [1]. Most patients are able to undergo surgery and thereafter receive adjuvant chemotherapy, radiotherapy and hormone therapy to reduce the risk of relapse [2]. Surgery can be breast-conserving surgery (BCS) or mastectomy with axillary lymph node (ALN) resection [3]. Many study-related prognostic factors like tumor size, hormone receptor status, c-erbB overexpression and metastatic lymph node status have been established to predict the relapse risk and to deter-

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0030–2414/10/0792–0105$26.00/0

Accessible online at:
www.karger.com/ocl

Bala Basak Oven Ustaalioglu, MD
Selimiye Mah, Şair Nesimi sok, Kardeşler Apt.
No: 1, Daire: 4, 34668, Uskudar
TR–34668 Istanbul (Turkey)
Tel. +90 505 540 1630, Fax +90 216 442 29 47, E-Mail basakoven@yahoo.com

mine the best adjuvant therapy [2, 3]. Metastatic ALNs are the most important prognostic factor and if the number of positive lymph node increases, the mortality rate increases in breast cancer [3–5]. According to the 6th edition of the American Joint Committee on Cancer (AJCC) staging system, patients with 1–3 positive ALNs have been classified as N1, patients with 4–9 positive ALNs have been classified as N2, and patients with ≥10 positive ALNs have been classified as N3 [6]. Surgical procedure or pathological evaluation can affect the number of involved lymph nodes; therefore, if ALN dissection is insufficiently performed, it is difficult to correctly determine the N classification. It may thus add to the confusion in the prognostic system, taking into consideration both the involved and all the examined lymph nodes [5]. The ratio of the number of metastatic lymph nodes over the total number of resected lymph nodes that is called 'metastatic lymph node ratio' (n ratio) has been reported as prognostic factor for several malignancies like stomach, pancreas and colon cancers [7–9]. The n ratio has also been reported as an important prognostic factor for breast cancer and it has been found to improve prognosis compared with the pN stage [2, 4, 10–13].

There have been several studies including a heterogeneous group of patients who were operated and treated by different surgeons and oncologists [14] which may affect the results. In this study, we report whether the n ratio is important in predicting disease-free survival (DFS) in breast cancer patients with ALN metastasis who have been operated on in our center. In addition, the relation between the n ratio and clinicopathological characteristics was also studied.

Material and Methods

From May 1999 to March 2009, data of 802 breast cancer patients who were treated in our oncology department at Dr. Lutfi Kirdar Kartal Education and Research Hospital were available. We selected 427 breast cancer patients who had ALN metastasis and underwent modified radical mastectomy or BCS with ALN resection. All pT stages were included. Patients who received neoadjuvant chemotherapy were not excluded. Patients with distant metastases at diagnosis and patients with secondary malignancies except for non-melanoma skin cancer or in situ cervix cancer were excluded from the study. Lymph node involvement was classified according to the AJCC TNM classification (N1, 1–3 metastatic lymph nodes; N2, 4–9 metastatic lymph nodes; N3, ≥10 metastatic lymph nodes). This is a retrospective, observational and review-based study of medical records of patients in our institutions.

Clinical information about age, operation type, tumor location, histopathology, tumor stage, tumor size, histological grade, multicentricity, necrosis, extracapsular invasion, lymph node involvement, lymphatic, perineural and vascular invasion, hormone receptor status, c-erbB overexpression, adjuvant chemotherapy, radiation therapy, hormone therapy, trastuzumab therapy, responses to treatment and survival were obtained from patients' charts.

The ratio between the positive and the dissected lymph nodes was determined by the best cut-off approach in terms of the log-rank test. The n ratio was calculated as positive lymph node involvement divided by total lymph nodes dissected multiplied with 100, and this ratio was categorized as n ratio 1 (1–10%), n ratio 2 (10.01–50%) or n ratio 3 (>50%). The number of patients in each group was similar.

Statistical Analysis

Statistical analyses were performed using SPSS 17.0 (SPSS Inc., Chicago, Ill., USA) software. The analysis was done in 2 steps. First, we evaluated the prognostic importance of the n ratio and other prognostic factors. Survival analysis and curves were established according to the Kaplan-Meier method and compared by the log-rank test. DFS was defined as the time from surgery to the last follow-up, and the time until relapse was defined as the time from surgery to the first evidence of relapse. In addition, overall survival (OS) was described as the time from diagnosis to the date of the patient's death or last known contact. In a second step, we evaluated the relationship between the n ratio and other prognostic factors. The significance of the differences among the means was determined by the Mann-Whitney U test and Kruskal-Wallis test. Factors analyzed by univariate analysis were also examined with multivariate analysis using the Cox proportional hazards model to predict risk factors for relapse. Multivariate p values were used to characterize the independence of these factors. The 95% confidence interval (CI) was used to quantify the relationship between survival time and each independent factor. All p values were 2-sided in tests, and p values ≤0.05 were considered to be statistically significant.

Results

A total of 802 patients with breast cancer were evaluated retrospectively. Patients with distant metastases and patients without ALN involvement at the time of diagnosis were excluded from the study, and the remaining 427 patients were analyzed. Eighty-five patients (20%) relapsed after a mean of 35 months (range 4–220). A total of 138 patients (32.3%) underwent BCS, and modified radical mastectomy was performed in the other 289 patients (67.7%). All patients had histologically proven breast carcinoma: nearly 90% of patients had invasive ductal carcinoma, 6.3% invasive lobular carcinoma, 2.6% mixed-type carcinoma, and others. More than 90% of patients received adjuvant chemotherapy, 80% of patients received radiotherapy because of ALN involvement or

Table 1. Characteristics of the axillary lymph node dissection and n ratio

	Patients	5-year DFS rate
Resected lymph nodes		
1–10	91 (21.4)	76
11–20	246 (57.9)	66
21–30	72 (16.9)	61
>30	16 (3.8)	NA
Metastatic lymph nodes		
1–10	356 (84)	69
11–20	50 (11.8)	59
21–30	13 (13.1)	58
>30	5 (1.2)	NA
n ratio		
0–20%	157 (36.9)	76
21–50%	136 (32)	63
>50%	132 (31)	59

Figures in parentheses are percentages. NA = Not applicable.

Table 2. Correlation between the n ratio and clinicopathological characteristics

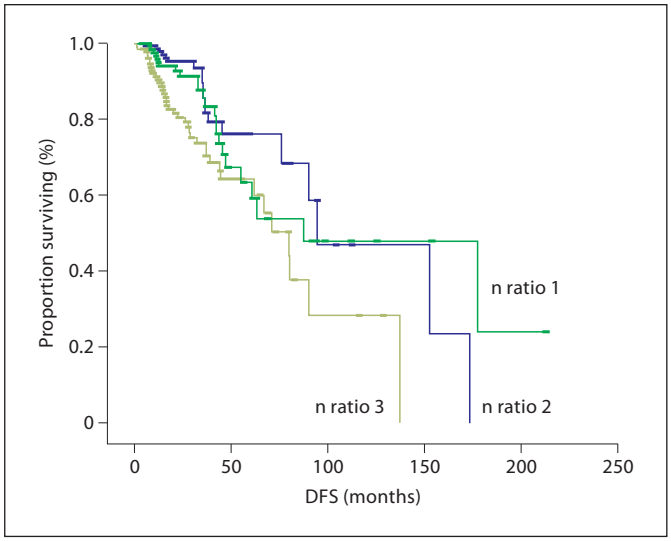
Variables		Patients	Mean n ratio ± SD	p value
Age	≤35 years	33	33.87 ± 24.50	0.5
	>35 years	380	36.45 ± 25.81	
T stage	T1	98	27.79 ± 23.86	<0.0001
	T2	242	35.84 ± 25.01	
	T3	53	42.05 ± 24.83	
	T4	26	52.58 ± 25.73	
N stage	N1	192	16.64 ± 15.14	<0.0001
	N2	155	43.72 ± 18.28	
	N3	78	69.10 ± 14.34	
Stage	II	170	16.34 ± 14.86	<0.0001
	III	255	49.34 ± 22.57	
Excised lymph nodes	1–10	91	44.90 ± 25.52	<0.0001
	11–20	246	32.69 ± 23.65	
	21–30	72	34.01 ± 27.21	
	>30	16	49.04 ± 33.28	
Menopausal status	Premenopausal	202	37.25 ± 26.18	0.53
	Postmenopausal	223	35.14 ± 25.07	
Grade	1	14	29.15 ± 21.00	0.05
	2	268	34.38 ± 25.36	
	3	143	40.14 ± 26.07	
Lympho vascular invasion	Present	254	39.36 ± 26.44	<0.0001
	Absent	107	27.34 ± 20.88	
Extracapsular invasion	Present	173	43.76 ± 24.30	<0.0001
	Absent	211	28.89 ± 24.45	
Multi centricity	Present	67	41.05 ± 26.73	0.14
	Absent	358	35.22 ± 25.31	
Perineural invasion	Present	166	38.39 ± 25.62	0.07
	Absent	156	33.68 ± 26.11	
Necrosis	Present	136	39.61 ± 26.33	0.13
	Absent	165	34.93 ± 25.31	
Estrogen receptor	Positive	277	34.71 ± 25.14	0.11
	Negative	125	39.42 ± 26.58	
Progesterone receptor	Positive	287	34.37 ± 25.39	0.01
	Absent	117	40.89 ± 25.42	
Triple negative	Present	33	36.42 ± 25.46	0.96
	Absent	378	36.36 ± 25.85	
Inflammatory cancer	Present	31	52.19 ± 26.86	0.001
	Absent	394	34.88 ± 25.09	
Neoadjuvant chemotherapy	Present	39	45.53 ± 23.05	0.005
	Absent	386	35.19 ± 25.67	

p values were analyzed by the Mann-Whitney U test for 2 variables, and the Kruskal-Wallis test was used for more than 2 variables.

BCS, and 90% of them were treated with adjuvant hormone therapy according to the hormone receptor status.

The median age was 50 years, ranging from 27 to 82 years. While 202 patients were premenopausal (47.3%), 225 patients were postmenopausal (52.7%). The median number of dissected and metastatic ALNs was 15 (range 1–55) and 6 (range 1–42), respectively. Based on the number of ALNs, 193 (45.2%) patients classified as pN1, 156 (36.5%) as pN2 and 78 (18.3%) as pN3. The majority of patients were classified as T2 (244 patients, 52.1%). Using the n ratio classification, 157 patients (36.9%) were classified as n ratio 1, 136 (32%) as n ratio 2 and 132 (31.1%) as n ratio 3. The mean n ratio continuous value was 36 (range 1–84). In the 85 relapsed patients, the mean n ratio was 46 (range 4–84). The characteristics of ALN dissection and n ratio are shown in table 1. The n ratio was significantly higher in patients with breast cancer with advanced pT stage, advanced stage, undifferentiated histology, lymphovascular invasion and extracapsular extension. In addition, the n ratio was significantly correlated with the number of ALN metastases, the presence of inflammatory breast cancer and positive progesterone receptor. The correlation between n ratio and clinicopathological characteristics is shown in table 2.

At the median follow-up of 35 months (range 4–220), 5- and 10-year DFS was 68 and 39%, respectively. The mean DFS time was 87.3 months (SE 6.1, 95% CI 75.3–



Color version available online

Fig. 1. Kaplan-Meier DFS curves for breast cancer patients according to n ratio groups.

99.2). The 5-year DFS rates were 76% for n ratio 1, 63% for n ratio 2 and 59% for n ratio 3, and the 7-year DFS rates were 68% for n ratio 1, 53% for n ratio 2 and 37% for n ratio 3, respectively, according to the n ratio classification (fig. 1). The median DFS for n ratios 1, 2 and 3 were 94.6, 87.3 and 79.9 months, respectively ($p = 0.005$).

In the univariate analysis, the presence of multicentricity ($p < 0.001$), histological grade ($p = 0.02$), necrosis ($p = 0.04$), pN stage ($p < 0.001$), clinical stage ($p < 0.001$), estrogen receptor ($p = 0.004$) and progesterone receptor ($p < 0.001$) positivity, trastuzumab usage ($p < 0.001$), inflammatory breast cancer ($p = 0.002$), neoadjuvant chemotherapy ($p = 0.001$) and n ratio ($p = 0.005$) were found to be important factors in predicting DFS. The results of the univariate analysis are shown in table 3. We carried out a multivariate analysis with the Cox proportional hazards model in order to further evaluate the prognostic significance of the n ratio. Multivariate analysis indicated that the presence of multicentricity ($p < 0.001$; hazard ratio, HR, 0.269; 95% CI 0.13–0.53), neoadjuvant chemotherapy ($p = 0.003$; HR 0.20; 95% CI 0.07–0.58), trastuzumab usage ($p < 0.001$; HR 0.25; 95% CI 0.11–0.52) and n ratio ($p = 0.02$; HR 1.03; 95% CI 1–1.07) were significantly associated with prognosis; table 4 shows the results of multivariate analysis. After categorization of the n ratio as n ratio 1 (1–10%), n ratio 2 (10.01–50%) and n ratio 3 (>50%), the significance of the n ratio in the multivariate analysis missed ($p = 0.06$; HR 1.03; 95% CI 0.1–1.05). Both pN stage and n ratio were analyzed, but pN stage lost its significance compared with the n ratio as prognostic factor in a multivariate analysis.

Discussion

Lymph node metastasis is one of the most important prognostic factors, and it is important in deciding whether adjuvant therapy is necessary or not [15]. Although the TNM staging classification has not been included in the n ratio, it is an alternative to the N stage in indicating lymph node status [15].

The positive nodes in the axilla are dependent on the type of axillary dissection performed and on the extent of the pathological examination [16]. In our study, all patients were operated and followed-up in our institutions using the same therapeutic protocols. Also, all surgical specimens obtained from the operations were evaluated at the pathology department in our institutions. Although the absolute number of metastatic ALNs was defined as important factor to predict relapse [17], the n ratio outweighed the pN stage by univariate and multivariate analysis in our study. Although the pN stage was statistically significant by univariate analysis, it was not supported by multivariate analysis. Megale Costa et al. [2] reported that the n ratio was an important prognostic factor to predict DFS for 168 breast cancer patients. Voordeckers et al. [3] also indicated that the n ratio was the most important factor, superior to the N stage, in 801 lymph node-positive breast cancer patients. We categorized the n ratio depending on the previous study of Voordeckers et al. [3]. Van der Wal et al. [13] reported that an n ratio ≥ 0.2 was associated with an increase in mortality in stage I and II breast cancer patients but they did not analyze the effect of the n ratio on DFS. Kuru [10] also analyzed the n ratio in breast cancer with T1–3 tumors and they found 0.25 as the cut-off value for the n ratio. In our study, we included all T stages, including inflammatory breast cancer. Truong et al. [11, 12] reported 2 studies related to the n ratio. In 1 study [11], they found that the n ratio was important for micrometastatic lymph node involvement. In another study [12], they evaluated T1–3 breast cancer patients, and the n ratio >0.25 was a poor prognostic factor both for OS and DFS. We analyzed the n ratio only for recurrence not for survival. Because of the short median follow-up time, we could not reach the median OS time. In all of these studies which evaluated the n ratio for prognostic factors, the n ratio had prognostic importance; however, in our

Table 3. Results of the univariate analysis

	Characteristics	n	Median DFS, months	95% CI	p
Menopausal status	Premenopausal	202 (47.3)	94.6	54.7–134.4	
	Postmenopausal	225 (52.7)	79.9	NA	0.25
Tumor localization	Right	214 (50.5)	94.6	37.9–151.2	
	Left	200 (47.2)	79.9	69.6–90.1	
	Bilateral	10 (2.4)	35	NA	0.88
Operation type	MRM	289 (67.7)	NA	NA	
	BCS	138 (32.3)	NA	NA	0.24
Multicentric site	Present	68 (15.9)	38.9	34.4–43.3	
	Absent	359 (84.1)	90.1	76.5–103.6	<0.001
Grade	1	14 (3.3)	NA	NA	
	2	268 (62.8)	94.6	51.2–137.9	
	3	145 (34)	70.9	47.3–94.5	0.02
Lymphovascular invasion	Present	255 (59.7)	80.1	60.7–99.5	
	Absent	107 (25.1)	152.6	58.9–246.2	0.837
Perineural invasion	Present	166 (38.9)	87.3	54.9–119.7	
	Absent	157 (36.8)	90.1	66.1–114	0.938
Necrosis	Present	136 (31.7)	79.9	55.8–103.9	
	Absent	165 (38.5)	152.6	88.2–216.9	0.04
T stages	T1	98 (23)	76.1	37.1–115	
	T2	244 (57.1)	90.3	80.8–99.8	
	T3	53 (12.4)	63.3	34.7–91.8	
	T4	26 (6.1)	44	15.6–72.3	0.06
N stages	N1	193 (45.2)	90.1	74.4–105.7	
	N2	156 (36.5)	177.6	NA	
	N3	78 (18.3)	61.9	27–96.8	<0.001
Extracapsular invasion	Present	136 (31.9)	137.3	63.2–211.3	
	Absent	165 (38.9)	76.1	48–104.1	0.136
Stage	II	171 (40.1)	94.6	71.8–117.3	
	III	256 (59.9)	79.9	62.2–97.5	<0.001
Estrogen receptor	Positive	278 (68.3)	90.1	69.4–110.7	
	Negative	126 (31)	76.1	35.8–116.3	0.04
Progesterone receptor	Positive	287 (70.5)	94.6	34.6–154.5	
	Negative	119 (29.2)	61.9	35.5–88.3	<0.001
c-erbB	+++	94 (24.3)	NA	NA	
	–	265 (68.5)	NA	NA	
	++	9 (2.3)	NA	NA	0.3
Trastuzumab usage	Present	58 (16.3)	42.3	23.3–61.4	
	Absent	298 (83.7)	90.3	36.5–144.1	<0.001
Triple negative	Present	33 (8)	87.3	18.2–156.4	
	Absent	380 (92)	79.9	161.5–98.2	0.6
Inflammatory breast cancer	Present	31 (7.3)	70.9	26.6–115.2	
	Absent	396 (92.7)	90.1	77.1–103	0.002
Adjuvant CT	Present	380 (92.2)	80.13	67.16–93.10	
	Absent	32 (7.8)	60.86	NA	0.88
Adjuvant RT	Present	331 (80.3)	80.13	57.6–102.59	
	Absent	81 (19.7)	87.33	73.19–101.4	0.19
Hormonotherapy	Present	306 (91.3)	90.10	75.56–104.6	
	Absent	29 (8.7)	87.33	26.7–147.96	0.82
Neoadjuvant CT	Present	380 (92.2)	NA	NA	
	Absent	32 (7.8)	87.3	75.2–99.4	0.014
n ratio	1	157 (36.9)	94.6	45.2–143.9	
	2	136 (32)	87.3	23.4–151.2	
	3	132 (31.1)	79.9	58.5–101.2	0.005

Figures in parentheses are percentages. NA = Not applicable; MRM = modified radical mastectomy; CT = chemotherapy; RT = radiotherapy.

Table 4. Results of the multivariate analysis

Characteristics	Wald	p	HR	95% CI
Multicentricity	14.229	<0.001	0.269	0.136–0.532
Grade	0.007	0.933	1.027	0.558–1.889
N stage	0.624	0.430	2.043	0.347–12.018
Stage (II vs. III)	0.315	0.575	2.717	0.083–89.407
Necrosis (present vs. absent)	1.502	0.220	2.673	0.555–12.886
ER (positive vs. negative)	0.075	0.784	0.904	0.439–1.862
PR (positive vs. negative)	2.384	0.123	1.743	0.861–3.529
Inflammatory breast cancer	0.477	0.490	0.652	0.193–2.197
Neoadjuvant chemotherapy	8.867	0.003	0.207	0.073–0.584
Trastuzumab treatment	13.486	<0.001	0.250	0.119–0.524
n ratio (categorical)	3.509	0.061	0.327	0.102–1.053
n ratio (continuous)	4.77	0.02	1.037	1.004–1.071

PR = Progesterone receptor; ER = estrogen receptor.

study, we also evaluated the correlation between the n ratio and other clinicopathological factors. We found that the n ratio was significantly greater in cases with undifferentiated tumor, a large tumor or advanced pT stage, lymphovascular invasion, extracapsular extension, progesterone receptor positivity, presence of inflammatory breast cancer and advanced clinical stage. In addition, the n ratio was significantly correlated with excised lymph nodes and the number of lymph node metastases. Vinh-Hung et al. [4] evaluated 1,827 breast cancer patients with all T and N stages which has been the largest study using the n ratio, and they reported that age, histological grade, tumor size, radiotherapy, chemotherapy, endocrine therapy and n ratio were important prognostic factors for breast cancer mortality. And also, n ratio continuous covariates were the most important prognostic factor in multivariate analysis. They used the n ratio in continuous variables to determine prognostic importance and then categorized the n ratio as low risk ($\leq$0.20), intermediate risk (0.20–0.65) and high risk (>0.65). They reported that breast cancer-specific survivals were 75.2, 63.3 and 39.6%, respectively, for low-, intermediate- and high-risk n ratio groups. Categorization of continuous variables has been shown to be associated with several problems like loss of information, loss of power and decrease in efficiency of survival analysis [18–20]. Similar to the study of Vinh-Hung et al. [4], we also used the n ratio as continuous variable in the survival analysis. After categorizing the n ratio, statistical significance was lost in the multivariate analysis. Hatoum et al. [14] evaluated the n ratio as categorical variable in lymph node-positive breast cancer and reported that the categorical n ratio was also an important prognostic factor for survival. Germain et al. [21] examined 3,000 breast cancer patients with all T stages, like in our study, and grouped the n ratio as 0.25, 0.25–0.5 and 0.5–0.8, reporting that the n ratio was an important prognostic factor for metastasis-free survival, compatible with our study. Martinez-Ramos et al. [15] reported that the n ratio was an important prognostic factor for DFS; in addition, their study was the first study using the population cancer registry in a European country. In another study, Katz et al. [22] showed that the n ratio was the strongest predictor for DFS and OS in 913 locally advanced breast cancer patients. Our results could be similar to the rest of Turkey because our oncology institute is the second high-capacity center in Istanbul and takes a lot of applications from rural areas. All of these studies similar to ours were retrospective. Two other prospective studies conducted by the Danish Breast Cancer Cooperative Group (the 77c and 82b study) demonstrated that the n ratio was significant in multivariate analysis [23, 24]. In the 77c study [23], the n ratio, examined continuously, was a predictor of DFS in postmenopausal patients with hormone receptor-positive status. In the 82b study [24], including stage II and III breast cancer patients, the n ratio was categorized and found to be important both for DFS and OS.

In the univariate analysis, both pN stage and n ratio were statistically significant to predict DFS ($p < 0.001$ and $p = 0.005$, respectively), and in the multivariate analysis, the n ratio continuous values maintained significant, with a hazard ratio of 1.037 ($p = 0.02$), whereas pN stage was not statistically significant ($p = 0.43$). In the multi-

variate analysis, pN stage was used as categorical variable but the n ratio was used as continuous variable. Thus, it was compatible with the literature [15]. This could have affected the results, but pN stage has to be used categorically according to TNM staging. After the n ratio was used categorically in the multivariate analysis, significance was lost ($p = 0.06$). This was the major limitation of our study. On the other hand, 39 patients who received neoadjuvant chemotherapy were not excluded from our study, which might have modified the nodal status in the axillary dissection [25].

Conclusions

The n ratio is an inexpensive, easily available and simple prognostic factor for breast cancer patients with positive ALNs. However, our study was retrospective, and this might lead to bias in the selection of patients. With longer follow-up, OS time can be reached in the future. We found the n ratio an important factor predicting DFS and it is noteworthy that all of our patients were operated and evaluated pathologically and treated in the same institution. In the future, the n ratio may replace the pN stage as prognostic factor.

References

1 Chu KC, Tarone RE, Kessler LG, et al: Recent trends in US breast cancer incidence, survival, and mortality rates. J Natl Cancer Inst 1996;88:1571–1579.
2 Megale Costa LJ, Soares HP, Gaspar HA, Trujillo LG, et al: Ratio between positive lymph nodes and total dissected axillaries lymph nodes as an independent prognostic factor for disease-free survival in patients with breast cancer. Am J Clin Oncol 2004;27:304–306.
3 Voordeckers M, Vinh-Hung V, Van de Steene J, et al: The lymph node ratio as prognostic factor in node-positive breast cancer. Radiother Oncol 2004;70:225–230.
4 Vinh-Hung V, Verkooijen HM, Fioretta G, et al: Lymph node ratio as an alternative to pN staging in node-positive breast cancer. J Clin Oncol 2009;27:1062–1068.
5 Vinh-Hung V, Verschraegen C, Promish DI, et al: Ratios of involved nodes in early breast cancer. Breast Cancer Res 2004;6:680–688.
6 Singletary SE, Allred C, Ashley P, et al: Revision of the American Joint Committee on Cancer staging system for breast cancer. J Clin Oncol 2002;20:3628–3636.
7 Caigang L, Ping L, Yang L, et al: Clinical implications of metastatic lymph node ratio in gastric cancer. BMC Cancer 2007;7:200.
8 Slidell MB, Chang DC, Cameron JL, et al: Impact of total lymph node count and lymph node ratio on staging and survival after pancreatectomy for pancreatic adenocarcinoma: a large, population-based analysis. Ann Surg Oncol 2008;15:165–174.
9 Wang J, Hassett JM, Dayton MT, Kulaylat MN: Lymph node ratio: role in the staging of node-positive colon cancer. Ann Surg Oncol 2008;15:1600–1608.
10 Kuru B: Prognostic significance of total number of nodes removed, negative nodes removed, and ratio of positive nodes to removed nodes in node positive breast carcinoma. Eur J Surg Oncol 2006;32:1082–1088.
11 Truong PT, Vinh-Hung V, Cserni G, et al: Member of the International Nodal Ratio Working Group. The number of positive nodes and the ratio of positive to excised nodes are significant predictors of survival in women with micrometastatic node-positive breast cancer. Eur J Cancer 2008;44:1670–1677.
12 Truong PT, Berthelet E, Lee J, Kader HA, Olivotto IA: The prognostic significance of the percentage of positive/dissected axillary lymph nodes in breast cancer recurrence and survival in patients with one to three positive axillary lymph nodes. Cancer 2005;103:2006–2014.
13 van der Wal BC, Butzelaar RM, van der Meij S, Boermeester MA: Axillary lymph node ratio and total number of removed lymph nodes: predictors of survival in stage I and II breast cancer. Eur J Surg Oncol 2002;28:481–489.
14 Hatoum HA, Jamali FR, El-Saghir NS, et al: Ratio between positive lymph nodes and total excised axillary lymph nodes as an independent prognostic factor for overall survival in patients with nonmetastatic lymph node-positive breast cancer. Ann Surg Oncol 2009;16:3388–3395.
15 Martinez-Ramos D, Escrig-Sos J, Alcalde-Sanchez M, Torrella-Ramos A, Salvador-Sanchis JL: Disease-free survival and prognostic significance of metastatic lymph node ratio in T1-T2 N positive breast cancer patients. A population registry-based study in a European country. World J Surg 2009;33:1659–1664.
16 Woodward WA, Vinh-Hung V, Ueno NT, et al: Prognostic value of nodal ratios in node-positive breast cancer. J Clin Oncol 2006;24:2910–2916.
17 Carter CL, Allen C, Henson DE: Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. Cancer 1989;63:181–187.
18 Holländer N, Schumacher M: On the problem of using 'optimal' cutpoints in the assessment of quantitative prognostic factors. Onkologie 2001;24:194–199.
19 Morgan TM, Elashoff RM: Effect of covariate measurement error in randomized clinical trials. Stat Med 1987;6:31–41.
20 Schmoor C, Schumacher M: Effects of covariate omission and categorization when analysing randomized trials with the Cox model. Stat Med 1997;16:225–237.
21 Germain I, Fortin A, Dagnault A: The value of the number of nodes removed (or the ratio of involved nodes) as a prognostic factor in breast cancer. Proc Am Soc Clin Oncol 2004;23:abstract 611.
22 Katz A, Buchholz TA, Thames H, et al: Recursive partitioning analysis of locoregional recurrence patterns following mastectomy: implications for adjuvant irradiation. Int J Radiat Oncol Biol Phys 2001;50:397–403.
23 Overgaard M, Jensen MB, Overgaard J, et al: Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. Lancet 1999;353:1641–1648.
24 Knoop AS, Bentzen SM, Nielsen MM, Rasmussen BB, Rose C: Value of epidermal growth factor receptor, HER2, p53, and steroid receptors in predicting the efficacy of tamoxifen in high-risk postmenopausal breast cancer patients. J Clin Oncol 2001;19:3376–3384.
25 Baslaim MM, Al Malik OA, Al-Sobhi SS, et al: Decreased axillary lymph node retrieval in patients after neoadjuvant chemotherapy. Am J Surg 2002;184:299–301.