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ORIGINAL ARTICLE

Dissection axillary lymph node count in patient with breast cancer followed by neoadjuvant therapy

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Abstract

Introduction: Breast cancer is the most common cancer and the second cause of death in women. It is essential to have the highest level of confidence in axillary staging assessment. Many surgeons and pathologists believe that fewer lymph nodes are present in axillary dissection specimens of women treated by neoadjuvant chemotherapy. Consequently, the purpose of this study was to compare the lymph node counts of axillary dissection specimens from patients having received neoadjuvant chemotherapy with those of patients treated with primary operation.

Methods: This descriptive study was conducted on 100 women with invasive breast cancer who underwent level I and II axillary lymph node dissections from 2012 through 2013 in Quaem hospital surgery department . these patients dichotomized into two categories: Women from the neoadjuvant chemotherapy group (n=50) were compared with those from the primary surgery group (n=50). The total number of lymph nodes harvested was compared ,the obtained data was analyzed by SPSS software (V: 16), using Kruskal-Wallis and Mann-Whitney at the significant level P<0/05..

Results: range of age in Neoadjuvant and Surgery group respectively was 23–68 and 26–89 years. The median number of lymph nodes retrieved in the neoadjuvant chemotherapy group was 14.0 (range 5 to 25) compared with 16 (range 5 to 32) in Surgery-first group, although there was not statistically significant difference between the two groups (P=0.122). Tumor stage and nodal stage were significantly higher in the neoadjuvant group (p≤0.001).

Conclusions: This study suggests that administration of neoadjuvant chemotherapy to breast cancer patient's results in a reduced number of lymph nodes retrieved in the axillary dissection specimens.

Key Words: Breast cancer; Axillary Lymph node Dissection; Neoadjuvant therapy; chemotherapy

Introduction

Breast cancer is of the most prevalent human cancers. Nowadays, considerations in to the conservative treatments such as chemotherapy and breast conservative procedures, has been increased [1]. In patients with Locally Invasive Breast Cancer (LABC), neoadjuvant chemotherapy has become the preferred initial treatment modality, followed by definitive surgical therapy directed to the breast and the axilla [2] and it is documented that the efficacy of this kind of treatment may be equal to other invasive therapy, if the patients selection, done, properly. On the other hand, accurate staging is essential in the accurate patient selection for this treatment. Traditional staging of the axilla in patients with LABC has involved a surgical level I and II or level I, II, and III Axillary Lymph Node Dissection (ALND) and a minimum of 10 lymph nodes is required in

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the ALND specimen for the dissection to provide accurate information for staging [3]. It is thought that neoadjuvant chemotherapy may reduce the number of tumor-involved lymph nodes, and so overall lymph node count in an ALND specimen, and may affect the estimation of the stage of breast cancer [4]. In this study, using an institutional series of neoadjuvant and non-neoadjuvant patients, we determined the Dissection axillary lymph node count in patient with breast cancer followed by neoadjuvant therapy.

Methods

Patients

In this descriptive study, Patients with breast cancer, who underwent ALND, at the University of Mashhad, Quaem hospital surgery department, from 2012 through 2013 were investigated. The patients divided in to two groups. Group 1: following completion of neoadjuvant chemotherapy, eligible patients underwent definitive breast cancer surgery. Group 2: Only underwent definitive breast cancer surgery. The two groups underwent a level I and II ALND. Patients in the former group were treated on the institutional protocols during that time, which included Doxorubicin-based therapy with or without additional Taxane (135 mg/m2) in the neoadjuvant setting in two to three weeks before ALND. The surgery group was the patients with breast cancer diagnosed in the 1-2 months before. We excluded the patients who underwent SNLB prior to starting chemotherapy from our analyses so that we would have a homogenous group of patients for whom all of the lymph nodes were exposed to chemotherapy prior to dissection. To control for variation of surgical technique, only patients who underwent ALND by a general surgeon with extensive experience in breast surgery were included for evaluation. Sample size was estimated according to the Neuman study(2006)[5] and by NCSS&PASS software.

Pathology

All ALND specimens were evaluated by pathology in accordance with the Quaem Department of Pathology guidelines. The standard procedure included careful gross dissection of the ALND specimen to identify and remove all palpable lymph nodes. Each lymph node was submitted in its entirety for histologic evaluation. For all cases repeat gross and visual inspection was performed before the final node count was reported. The total number of nodes represents both involved and uninvolved nodes recovered in the ALND specimen.

Statistics

Mann-Whitney U test was used to compare the number of nodes in the neoadjuvant and adjuvant groups was performed. The Kruskal-wallis test was used to test for ordered differences among the tumor (T) and node (N) staging categories by neoadjuvant and surgery and for the difference in proportion (or percentage) of patients who had different lymph node counts, retrieved at ALND between the neoadjuvant and surgery groups. Statistical analyzes were performed with SPSS statistical software, Version 11/5.

Results

A total of 50 neoadjuvant and 50 non-neoadjuvant patients were included. All the patients were present till the end of survey. range of age in Neoadjuvant and Surgery groups respectively was 23–68 and 26–89 years and there was no significant difference in age of the patients , between the two groups (p=0.4) .16% of the patients had family history of breast cancer. 97 patients (97%) had invasive ductal and 3% had invasive lobular breast cancer. The median number of lymph nodes retrieved by ALND was 14 (5-32) in the neoadjuvant group and 16 (5-25) in the surgery group. There was no significant difference in the nodes retrieved between the two groups (P=0.122). Median size of the tumor was 36 mm and there was significant difference in size of tumor between the two groups ($p \leq 0.001$). In 64% of patients, the lymph nodes extracted were in the right side. Surgery patients were significantly older than the neoadjuvant patients (median age 55 vs. 47 years, $P = .043$). As expected, patients receiving neoadjuvant chemotherapy were more likely to have involved lymph nodes compared to the surgery group (Table 1). However, there was significant relationship between the total lymph nodes retrieved and the patients' node counts. Most of the patients (48%) in the Neoadjuvant group were in T3 and in the Surgery group were in T2 (42%). Most of the patients in the neoadjuvant group (50%) were in N2 nodal stage and tumor stage of IIIC (38%).There was significant statistical difference in the nodal stage and also tumor stage between the neoadjuvant and surgery groups ($p \leq o.oo1$). Patient and tumor characteristics are listed in Table 1 .

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Table 1: Patient and tumor characteristics

variable		Neoadjuvant group	Surgery group	P value
No. of patients		50	50	-
Median age, y (range)		47 (23–68)	55 (26–89)	0.043
Tumor stage	T0	2 (4%)	3 (6%)	≤0.001
	T1	5 (10%)	18 (36%)	
	T2	5 (10%)	24 (42%)	
	T3	24 (48%)	5 (10%)	
	T4	14(28%)	3(6%)	
Node Stage	N0	2 (4%)	3 (6%)	≤0.001
	N1	11(22%)	32 (64%)	
	N2	25 (50%)	11 (22%)	
	N3	12 (24%)	4 (8%)	
Median lymph nodes retrieved		14	16	-

Discussion

Accurate staging of the axilla in breast cancer,has important prognostic and therapeutic implications. For this reason mean lymph nodes retrieved by ALND procedure is of great importance. However this concept may not hold true for patients who have received neoadjuvant chemotherapy [6]. Although we did not find any difference in the median number of nodes retrieved, between patients treated with neoadjuvant chemotherapy and those treated with surgery, Fisher et al found a small, but statistically significant, difference in the median number of nodes retrieved [7]. The same as our study , Neoman et al. suggested that there are lower lymph nodes retrieved in the patients on neoadjuvant chemotherapy compared with the surgery group [8]. Basleim et al. also reported decrement in the nodes retrieved after neoadjuvant chemotherapy [9]. But, Hunt et al. found no significant difference between the neoadjuvant patients and surgery only ones [10]. Straver, also found no significant difference in the mean nodes retrieved in the neoadjuvant group and surgery group [11]. Cil et also, found similar results [12]. There are several possible mechanisms by which neoadjuvant chemotherapy could result in a low lymph node recovery rate. Neoadjuvant chemotherapy has been shown to cause regression in the degree of disease found within the axilla [7]. Pathologic reviews of the primary tumor and axilla in patients who have undergone neoadjuvant chemotherapy , have found an increased fibrous stromal response in the tumor and surrounding tissue [13]. Alternatively, neoadjuvant chemotherapy may directly obliterate the lymph nodes by being cytotoxic to the lymphocytes, which constitute the vast majority of the lymph node cortex.

We controlled for other factors that might explain differences in lymph node retrieval, and may cause bias in the study , including the surgical technique used for nodes extraction and pathologic methods for nodes retrieval. Previous studies have identified higher nodes retrieved from surgeons with an academic affiliation or in a teaching hospital setting [14]. Makris et al. reported different number of lymph node retrived between pathologists and pathology residents [15].We used a single trained surgeon and also single pathologist. Inadequate pathology processing could also be another explanation for low lymph node retrieval; however all patients had repeat gross and visual inspection performed by the pathologist, before the final node count was reported, making this explanation unlikely.

Previous studies evaluating ALND have noted a decreased number of nodes retrieved in elderly patients [16], and therefore we evaluated patient age to see if this could account for lower number of lymph nodes retrieved in patients receiving neoadjuvant chemotherapy. In our population, the patients receiving neoadjuvant therapy were found to be younger than the surgery-first group, and therefore advanced age cannot explain our findings. similarly, in the Calcut study ,the patients in the neoadjuvant therapy were younger [17].

In addition, several reports suggest that the likelihood of identifying axillary metastases increases with the number of lymph nodes recovered in an axillary lymph node specimen [18]. If so, we would have expected a higher total lymph node count among the higher stage, more nodally involved patients seen in the neoadjuvant group. In other studies like our survey, patients in the neoadjuvant group had higher nodal and tumoral stage. The nodes retrieved is also may be affected by the nodal and tumoral stage [14, 16]. In some other study there was also level 3 of ALND that results in more lymph node retrieved [19](We did ALND in level 1 and 2).

Conclusions

When a level I and II ALND is performed, less mean lymph nodes, may be retrieved, in patients who have received neoadjuvant chemotherapy .This necessarily does not imply inadequate surgical staging. Also, this fact should be kept in the surgeons mind and equivoque more, in the surgery field, for any remnant lymph nodes. Also we re-emphasize on the advantage and importance of

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sentinel lymph node biopsy, because of adding more information in these circumstances. As the low volume of patients studied in our study ,Larger scale and multi centric surveys for the documentation of our finding are needed.

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