Is axillary lymph node dissection necessary for positive preoperative aspiration cytology lymph node results?

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Abstract

Introduction: Based on international guidelines, axillary lymph node dissection (ALND) is recommended in cases of breast cancer if preoperative examinations confirm axillary metastasis. We examined which set of preoperative parameters might render ALND unnecessary.

Patients and methods: Preoperative examinations (axillary ultrasound and aspiration cytology) confirmed axillary metastasis in 190 cases out of 2671 patients with breast cancer; primary ALN dissection was performed on these patients with or without prior neoadjuvant therapy. The clinicopathological results were analysed to determine which parameter might predict the presence of no more than 2 or 3 metastatic ALNs.

Results: The final histological examination confirmed 1–3 metastatic lymph nodes in ALND samples in 116 cases and over 3 metastatic lymph nodes in 74 cases.

For patients receiving neoadjuvant therapy (59 out of the 190 cases), if the size of the primary tumour was 2 cm or smaller and/or the metastatic ALN was 15 mm or smaller, then the patient was likely to have no more than 3 positive ALNs (stage N0–1 disease) ($p < 0.001$). If the patient did not receive neoadjuvant therapy, stage N2 or N3 disease was very likely. No correlation was found between other clinicopathological characteristics of the tumour and involvement of the ALNs.

Conclusion: Axillary lymph node dissection is not necessary for selected breast cancer patients with axillary metastasis receiving neoadjuvant therapy. In these cases, sentinel lymph node biopsy with or without radiation therapy and close follow-up may serve as adequate therapy.

Keywords: breast cancer, axillary lymph node dissection, neoadjuvant therapy, axillary metastasis

Introduction

Surgical treatment of patients with breast cancer and positive axillary lymph nodes is becoming less and less invasive. In the background, it would have been better to mention which are known high risk features that mandate ALND: The clinically node-positive axilla, confirmed by fine needle aspiration or core biopsy, in a patient for whom neoadjuvant chemotherapy is not planned. Occult breast cancer presenting as axillary node metastasis. SLN positive patients who fall outside the Z0011 selection criteria (i.e. >2 SLN positive, matted nodes, mastectomy, or breast conservation without whole-breast radiotherapy). Inflammatory, clinical stage T4, or high-risk T3 breast cancer. Failed SLN mapping. Inadequate prior ALND with residual clinically suspicious nodes Sentinel or axillary nodes which remain positive after neoadjuvant chemotherapy. Axillary recurrence following previous breast cancer treatment.

Based on results from the ACOSOG Z0011 study, axillary lymph node dissection (ALND) is not required even in cases with 1 or 2 axillary sentinel lymph nodes involving macrometastasis if the patient meets the inclusion criteria for the study.[1,2] This recommendation has been approved by international and Hungarian consensus conferences as well.[3,4]

Patients with ALN metastasis confirmed by preoperative examinations represent a separate treatment group. ALND must be performed on these patients if surgical treatment is required. Axillary ultrasound is a key method for diagnosing axillary metastasis, and a positive axillary ultrasound result also necessitates aspiration cytology. Sensitivity of axillary ultrasound ranges from 25 to 71% depending on the immunohistochemical status of the tumour[5]; sensitivity increases to approximately 70 to 80% with the addition of fine needle aspiration cytology (FNAC). [6,7,8,9]

In cases where a lymph node is found to be positive with aspiration cytology, systemic neoadjuvant therapy is performed on some patients. Based on international results, complete axillary pathological regression occurs in a significant portion of these patients.[10,11,12]

Two major prospective study has investigated SLNB after NAC: the SAKK 23/16 TAXIS trial and the ALLIANCE A011202 trial.

Similarly, we know that in a portion of patients, metastasis is only present in the sentinel lymph node. A study published in 2017 confirmed that axillary lymph node dissection is may not necessarily indicated as the first surgery; sentinel lymph node biopsy (SLNB) is recommended instead if the primary tumour is ≤2 cm as confirmed by a preoperative breast ultrasound examination, no more than one lymph node in the axillary region is confirmed positive with aspiration cytology, and the patient does not receive neoadjuvant therapy.[13]

Therefore, in our study, we were looking for correlations between the preoperative axillary ultrasound examination and clinicopathological factors to be able to predict not only the presence, but also the severity of axillary metastasis (slight or severe). A further aim of our study was to decide in advance when ALND is required and in which cases SLNB is sufficient based on the results of preoperative examinations.

Patients and methods

Pre- and postoperative data from 2671 cases where surgery was performed due to early invasive breast tumour were evaluated in the Department of Surgery, Faculty of Medicine, University of Szeged between 1 January 2007 and 31 December 2017. Mandatory items of the complex breast examination included a physical examination, an ultrasound examination, a mammogram and histology. This was a retrospective analysis of a prospectively maintained database.

Both axilla examined - axilla level 1,2,3 included- during the axillary US. All the enlarged and abnormal lymph nodes have to be recorded in the description. Axillary ultrasound was considered positive if the eccentric or concentric cortical region of the lymph node was larger than 2.5 mm, the adipose hilum was missing, the lymph node was morphologically rounded, or its blood supply was increased. In cases where axillary ultrasound and aspiration cytology were positive, neoadjuvant systemic therapy was also administered in some patients. Neoadjuvant therapy was administered in accordance with current international practice, primarily to be able to remove tumours originally found to be oncologically inoperable and to be able to perform breast-conserving surgery instead of a mastectomy.

Surgical treatment: our goal was to provide locoregional tumour control and precise locoregional staging. With an aesthetic outcome also taken into consideration, breast-conserving surgery was performed whenever possible. ROLL (radio-guided occult lesion localisation) and dual labelling were used to localise breast tumours and the sentinel lymph node. At least 4 hours before the surgery, isotope (99mTc) labelled human colloidal albumin was administered into the lesion, which was followed by lymphoscintigraphy to determine the projection of the sentinel lymph node and that of the lymphatic drainage. As a first step during surgery, Patentblau dye was administered around the areola, and then manual gamma probe was used to remove the tumour and the sentinel lymph node(s) during the same procedure approximately 10 minutes later. ALND was primarily performed with or without prior neoadjuvant therapy if preoperative examinations confirmed the presence of even one axillary lymph node metastasis.

Patients were divided into two large groups on the basis of a final histological examination of the axillary lymph nodes. One group consisted of patients with no more than 3 positive lymph nodes (N0–1) in accordance with the TNM classification; the other group consisted of patients with 4 or more positive lymph nodes (N2–3). Due to the maximum of 2 positive lymph nodes described in the Z0011 study, we formed an additional group with no more than 2 metastatic lymph nodes (Z1) and another with 3 or more metastatic lymph nodes (Z2). The clinical, radiological and histological results of these groups were analysed as well.

In our study, clinicopathological results (histological and immunohistochemical status, tumour location, tumour size before and after surgery, size and number of abnormal lymph nodes described by ultrasound examination, cytology of the axillary lymph node, neoadjuvant therapy and final axillary histological lymph node status) were compared. We aimed to ascertain which preoperative examination results may be used to predict the presence of a maximum of only 2 or 3 metastatic lymph nodes in the axillary region.

Statistics IBM SPSS Statistics v22 software was used for statistical analysis in our study. Continuous variables were presented as mean and standard deviation, while categorical variables were presented as case number and percentages. The chi square test followed by logistic regression was used to evaluate the cumulative effect of the variables on axillary status. The difference was considered statistically significant in cases where $p < 0.05$ with 95% confidence interval.

Results

Surgical intervention was performed in 2671 invasive breast tumour cases (average age: 59.73 years). In 260 cases, axillary ultrasound suggested a metastatic lymph node; therefore, aspiration cytology sampling was performed. In 190 cases, pathology reports suggested metastasis; in these cases, ALND was performed. The average number of lymph nodes removed was 13.49.

False positive results were found in 11 (8.4%) of the 131 aspiration cytology examinations in patients not receiving neoadjuvant therapy. Based on a final histological examination of the ALNs, 76 (58%) patients were confirmed to be stage N0–1 and 55 (42%) patients were stage N2–3.

No significant correlation was found between preoperatively assessable clinicopathological parameters and axillary lymph node status for patients not receiving neoadjuvant therapy (Tables 1 and 2).

Neoadjuvant therapy was administered in 59 cases, and in 23 (39%) of these cases, complete axillary pathological remission was confirmed. Based on a final histological examination of the axillary lymph nodes, 40 (68%) patients were in stage N0–1 and 19 (32%) patients were in stage N2–3.

The results of the histological examinations, the immunohistochemical status and the number of positive lymph nodes detected by ultrasound examination showed no correlation to the final histological status of the lymph node. If preoperative ultrasound examinations find that the primary breast tumour is ≤20 mm ($p = 0.002$) or the positive lymph node is ≤15 mm ($p = 0.04$), the status of the axillary lymph nodes will likely be stage N0–1; therefore, a maximum of 3 positive axillary lymph nodes are present (Tables 3 and 4).

In patients with TNBC (triple negative breast cancer) who receiving neoadjuvant therapy if the size of the tumour is ≤20 mm based on the ultrasound examination is no more than 3 metastatic lymph nodes (N1, $p<0.001$) (Table 3).

We examined the likelihood of stage N0–1 in the presence of two preoperative factors: ≤20 mm tumour size as measured by ultrasound and a ≤15 mm size of the lymph node considered metastatic. In the patient group not receiving neoadjuvant therapy ($p = 0.948$), this could not be confirmed; however, in patients receiving neoadjuvant therapy, the likelihood of no more than 3 metastatic lymph nodes is very high ($p = 0.01$).

Logistic regression was used to examine which variables are predictive of axillary status. Using the omnibus test, we found that the independent variables in the model are more related to the dependent variable than we would expect due to chance ($p < 0.001$). We were able to confirm that the size of the tumour (Exp (B) = 1.050, 95% CI = 1.016–1.085, $p = 0.004$) is predictive of axillary status. The resulting model was statistically significant ($\chi^2 = 18.806$, $df = 3$, $p < 0.001$). The proportion of cases categorized correctly was 69.4% (overall percentage) with this model, leading to a more precise result compared to categorizing by chance (55.4%) (Table 5).

Cases with no more than 2 (Z1) or 3 or more lymph nodes (Z2) were compared to the preoperatively assessable factors in patients grouped by receiving or not receiving neoadjuvant therapy. In patients not receiving neoadjuvant therapy, the size of the breast tumour, axillary status and clinicopathological characteristics of the tumour showed no correlation to the final histological status of the axilla (data not shown).

In patients receiving neoadjuvant therapy, the possibility of no more than 2 metastatic lymph nodes is very high if the size of the tumour is ≤20 mm ($p = 0.008$) based on the ultrasound examination and this is higher in patients with TNBC ($p=0.002$). The joint presence of two

preoperatively assessable factors – ≤20 mm tumour size confirmed by ultrasound and a ≤15 mm size of the lymph node considered metastatic – only increased the possibility of no more than 2 positive lymph nodes in patients receiving neoadjuvant therapy ($p = 0.728$ vs. $p = 0.017$) (Table 6).

The final lymph node status of the axilla showed no relation to other clinicopathological characteristics (data not shown).

Discussion

ALND has been the standard procedure in the surgical treatment of malignant breast tumours for at least 100 years, with significant changes occurring in recent years. SLNB[14] can be used to avoid ALND in a significant proportion of patients; therefore, morbidity of surgical treatment of early breast cancers can be decreased significantly.[15,16,17] At first, if preoperative examinations found no metastasis but the intraoperative or final histological examination confirmed metastasis in the SLN, ALND was considered necessary. Later, clinical studies confirmed that even the presence of micrometastasis or an isolated tumour cell in a lymph node is sufficient to indicate SLNB.[18,19] The result of the ACOSOG Z0011 study was a milestone. This study concluded that even in cases with a maximum of two positive lymph nodes containing macrometastasis, ALND may be avoided if the patient meets the inclusion criteria for the study.[1,2] Moreover, based on the results of the AMAROS study, ALND may also be avoided in patients who have undergone a mastectomy and have a SLN with confirmed metastasis; irradiation of the axillary region and close follow-up are sufficient.[20]

Nowadays, the effort to further limit the indication area of ALND accompanied by significant morbidity is completely reasonable. One way to do this is to preoperatively screen patients only at stage N1 axillary status. Based on several international guidelines, a sentinel lymph node biopsy should be performed in cases characterised by the presence of axillary lymph nodes considered negative by preoperative examinations and aspiration cytology or core biopsy should be performed with axillary lymph nodes considered positive.[3,4,21,22] Several research groups have studied which factors detected or examined during the preoperative period (imaging studies, histological finding etc.) may be suitable to determine whether SLNB or ALND should be performed during surgery.[13,23,24] In the post-Z0011 period of the treatment of breast tumours, not only the presence of axillary metastasis is examined, but positive cases are also differentiated as mild (lymph node status N1 and 1 to 3 positive lymph nodes) and severe (lymph node status N2 and 4 or more positive lymph nodes) axillary metastases. Lim et al. confirmed that if the patient meets the criteria for the Z0011 study and the axillary ultrasound

detects 3 or more positive lymph nodes, it is very likely that there are multiple positive lymph nodes in the axilla; therefore, ALND cannot be avoided.[23] This result has also been confirmed by Liu et al., who found that ALND may be avoided if patients meet the Z0011 study criteria and the axillary ultrasound examination confirms only one suspected metastatic lymph node[25]. If two lymph nodes are considered metastatic based on an ultrasound examination, histological sampling and axillary lymph node dissection are recommended. Liang et al. highlight the importance of a preoperative histological examination; the authors have shown that in cases where axillary lymph nodes are found to be positive with fine needle aspiration cytology, the patient is more likely to have more than 3 metastatic lymph nodes in the axilla, compared to cases where the sentinel lymph node biopsy confirms 1 to 2 metastatic lymph nodes.[26]

In our study, we examined which combination of preoperative parameters would allow axillary lymph node dissection to be avoided if axillary lymph node involvement is confirmed preoperatively. We also examined which of these clinicopathological characteristics could eliminate the need for this radical surgical intervention. Based on our results, the severity of the involvement of the axillary region in the tumour process could not be clearly predicted preoperatively with the clinicopathological characteristics of the tumour in patients not receiving neoadjuvant therapy. In contrast, a recent study confirmed that primary ALND is not necessary and SLNB is recommended if the preoperative breast ultrasound confirms a 2-cm or smaller primary tumour in the breast, no more than one positive lymph node is confirmed with aspiration cytology, and the patient does not receive neoadjuvant therapy.[13] In another retrospective study, Lloyd et al. also found that patients are very likely to have no more than 2 axillary lymph nodes with macrometastasis if the preoperative ultrasound confirmed a 20-mm or smaller primary tumour, histology of this tumour confirmed invasive ductal or lobular carcinoma, and breast-conserving surgery was performed. Therefore, in these cases, ALND represents overtreatment.[24]

Based on our study, we claim that lymph node status N0–1 in patients not receiving neoadjuvant therapy cannot be determined with certainty with preoperative examinations, while the lymph node status of patients receiving neoadjuvant chemotherapy can be predicted with great certainty based on the results of the preoperative ultrasound examination. If patients also receive neoadjuvant therapy, it can be predicted with high probability whether the disease is in stage N0–1 or not and whether ALND can be avoided or not based on the preoperative size of the tumour (<20 mm, $p = 0.002$) and the preoperative size of the lymph node (<5 mm, $p = 0.04$).

In patients with breast tumours, the lymph node status of the axilla plays a key role in planning local and systemic therapy. If there is a metastatic lymph node in the axilla, a

significant proportion of patients receive neoadjuvant systemic therapy, which resolves the axillary metastatic process in approximately 40% of cases.[27] Following neoadjuvant therapy, the standard surgical procedure in these patients was ALND even in cases with complete pathological remission. Several studies have addressed the question of sentinel lymph node biopsy and repeated biopsy after neoadjuvant therapy.[28] In the ACOSOG Z1071 study, the rate of false negative sentinel lymph node biopsies was close to 10% false negative (12.6%), and this value further decreased with the removal of the lymph node indicated with a marker (metal clip) during axillary core biopsy. During surgical intervention, the SLN is already detected using the classical dual tracer method (technetium 99m-labelled human colloidal albumin and blue dye). With this technique (targeted axillary dissection, TAD), the rate of false negative sentinel lymph nodes decreased to approximately 2%.[29,30,27,31] Pilewski et al. analysed data from 425 patients and studied the extent to which preoperative imaging studies influence the lymph node status of the axilla.[32,33] If the examinations suggested the presence of a metastatic lymph node and the patient met the criteria for the Z0011 study, axillary lymph node dissection could have been avoided in 71% of cases. If aspiration cytology was positive, ALND was unnecessary in 45% of cases. A Spanish study published in 2018 also investigated whether axillary lymph node dissection should be performed after neoadjuvant therapy in cases where an axillary lymph node is considered positive with aspiration cytology.[34] In cases showing a significant presence of the HER2 receptor and low expression of the oestrogen receptor, there is a high chance that complete pathological remission occurs, and in these cases, ALND was not recommended. Our analyses confirmed the same result. Following neoadjuvant therapy, no more than 3 and no more than 2 positive lymph nodes were confirmed, respectively, with the final histology in two-thirds (40/59, 68%) and in over 50% (34/59, 57%) of the cases, respectively; therefore, axillary lymph node dissection could have been avoided.

Data from 3398 patients were reviewed in a meta-analysis, and the authors aimed to see whether ALND is necessary after neoadjuvant therapy in lymph node-positive breast tumour cases.[10] According to the analysis, the recommended treatment strategy at present is ALND. However, optimizing preoperative examinations and screening the patient population may help to achieve a more precise preoperative evaluation of axillary lymph node status. In the future, performing SLN with the dual tracer method and labelling the positive axillary lymph node in advance with a metal clip or with a radiopharmaceutical containing iodine followed by removing the labelled lymph node may decrease the number of axillary lymph node dissections. Based on the analysis, HER2-positive and triple receptor-negative cases by immunochemistry require further research. A study published in 2017 showed that the efficacy of neoadjuvant

therapy did not differ in these cases, but further studies are recommended in these cases as well.[11] Our study also showed no correlation between the lymph node status and the immunochemical status of the tumour. The same result was found in a study; ALND could be avoided after neoadjuvant therapy in 48% of the patients, especially in the case of HER2 receptor-positive and triple receptor-negative cases. The study supported performing SLNB in patients with a breast tumour receiving neoadjuvant therapy and with multiple axillary lymph node metastases as well. Longer studies are required to support the results.[12] A retrospective study that processed data from 1944 patients confirms this result; the study concluded that if patients receive neoadjuvant therapy followed by a mastectomy and if the receptor status is HER2-positive and triple receptor-negative, ALND could most likely have been avoided.[35]

Conclusions

Our results show that detecting suspicious lymph nodes by axillary ultrasound examination may predict the stage of the disease; therefore, we consider a complete examination of the axilla important in ruling out potential lymph node metastases. Our results confirm that in patients receiving neoadjuvant therapy, in addition to the preoperative size of the tumour (<20 mm, $p = 0.002$), the preoperative size of the lymph node (<15 mm, $p = 0.04$) may also be used to predict that the stage of the disease is N0–1. In these cases, sentinel lymph node biopsy with or without radiation therapy and close follow-up may serve as adequate therapy.

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524 **Tables**

525

526 **Table 1.**

527 Relation of preoperative imaging results to final lymph node disease burden in patients not

528 receiving neoadjuvant therapy – I – Chi square test

529

Neoadj. 0	**N0–1 (n=76)**	**N2–3 (n=55)**	**p value**
Tumour size on imaging	n=76	n=55	0.703
≤20mm	44 (57.9%)	30 (54.5%)	
>20mm	32 (42.1%)	25 (45.5%)	
Tumour size on imaging (TNBC)	n=19	n=12	0.981
≤20mm	11 (57.9%)	7 (58.3%)	
>20mm	8 (42.1%)	5 (41.7%)	
Lymph node size on imaging	n=68	n=48	0.979
≤15mm	31 (45.6%)	22 (45.8%)	
>15mm	37 (54.4%)	26 (54.2%)	
Lymph node size on imaging (TNBC)	n=17	n=11	0.453
≤15mm	7 (41.17%)	3 (27.27%)	
>15mm	10 (58.83%)	8 (72.73%)	
Tumour ≤20mm and lymph node ≤15mm	n=31	n=22	0.948
Number of abnormal lymph nodes on axillary ultrasound	n=76	n=55	0.338
1	65 (85.53%)	43 (78.18%)	
>1	11 (14.47%)	12(21.82%)	

530

Table 2.

Relation of preoperative pathological factors to final lymph node disease burden in patients not receiving neoadjuvant therapy – II – Chi square test

Neoadj. 0	**N0–1 (n=76)**	**N2–3 (n=55)**	**p value**
ER	n=76	n=55	0.281
positive	47 (61.84%)	39 (70.91%)	
negative	29 (38.16%)	16 (29.09%)	
PR	n=76	n=55	0.305
positive	43 (56.58%)	36 (65.45%)	
negative	33 (43.42%)	19 (34.55%)	
Ki67	n=76	n=55	0.845
positive	64 (84.21%)	47 (85.45%)	
negative	12 (15.79%)	8 (14.55%)	
Topoiz.	n=76	n=55	0.883
positive	60 (78.95%)	44 (80%)	
negative	16 (21.05%)	11 (20%)	
HER-2	n=76	n=55	0.883
positive	16 (21.05%)	11 (20%)	
negative	60 (78.95%)	44 (80%)	
TNBC	n=76	n=55	0.672
yes	19 (25%)	12 (21.8%)	
no	57 (75%)	43 (78.2%)	
Tumour histology on biopsy	n=76	n=55	0.871
Ductal	48 (63.16%)	33 (60%)	
Lobular	4 (5.26%)	4 (7.27%)	
Other invasive	24 (31.58%)	18 (32.73%)	
Histologic grade	n=65	n=51	0.576
I	2 (3.08%)	3 (5.88%)	
II	27 (41.54%)	24 (47.06%)	
III	36 (55.38%)	24 (47.06%)	

Table 3.

Relation of preoperative imaging results to final lymph node disease burden in patients receiving neoadjuvant therapy – I – Chi square test

Neoadj.	**N0–1 (n=40)**	**N2–3 (n=19)**	**p value**
Tumour size on imaging	n=40	n=19	0.002
≤20mm	28 (70%)	5 (26.32%)	
>20mm	12 (30%)	14 (73.68%)	
Tumour size on imaging (TNBC)	n=16	n=7	<0.001
≤20mm	14 (87.5%)	0 (0%)	
>20mm	2 (12.5%)	7 (100%)	
Lymph node size on imaging	n=31	n=13	0.04
≤15mm	20 (64.51%)	4 (30.77%)	
>15mm	11 (35.49%)	9 (69.23%)	
Lymph node size on imaging (TNBC)	n=12	n=6	0.737
≤15mm	5 (41.67%)	3 (50%)	
>15mm	7 (58.33%)	3 (50%)	
Tumour ≤20mm and lymph node ≤15mm	n=20	n=4	0.01
Number of abnormal lymph nodes on axillary ultrasound	n=40	n=19	0.161
1	38 (95%)	15 (78.95%)	
>1	2 (5%)	4 (21.05%)	

Table 4.

Relation of preoperative pathological factors to final lymph node disease burden in patients receiving neoadjuvant therapy – II – Chi square test

Neoadj.	**N0–1 (n=40)**	**N2–3 (n=19)**	**p value**
ER	n=40	n=19	0.361
positive	16 (40%)	10 (52.63%)	
negative	24 (60%)	9 (47.37%)	
PR	n=40	n=19	0.432
positive	7 (17.5%)	5 (26.32%)	
negative	33 (82.5%)	14 (73.68%)	
Ki67	n=40	n=19	0.551
positive	31 (77.5%)	16 (84.22%)	
negative	9 (22.5%)	3 (15.78%)	
Topoiz.	n=40	n=19	0.305
positive	24 (60%)	14 (73.68%)	
negative	16 (40%)	5 (26.32%)	
HER-2	n=40	n=19	0.323
positive	11 (27.5%)	3 (15.78%)	
negative	29 (72.5%)	16 (84.22%)	
TNBC	n=40	n=19	0.816
yes	16 (40%)	7 (36.84%)	
no	24 (60%)	12 (63.16%)	
Tumour histology on biopsy	n=40	n=19	0.314
Ductal	29 (72.5%)	14 (73.69%)	
Lobular	0 (0%)	1 (5.26%)	
Other invasive	11 (27.5%)	4 (21.05%)	
Histologic grade	n=32	n=18	0.157
I	5 (15.62%)	0 (0%)	
II	12 (37.5%)	6 (33.33%)	
III	15 (46.88%)	12 (66.67%)	

Table 5.

Result of logistic regression

Variables	Sig	Exp(B)	95% CI for EXP(B)	
			Lower	Upper
Tumour size	0.004	1.050	1.016	1.085

Table 6.

Relation of imaging results to modified final lymph node disease burden (Z1 or Z2) in patients receiving neoadjuvant therapy – I – Chi square test

Neoadj.	**Z1 (n=34)**	**Z2 (n=25)**	**p value**
Tumour size on imaging	n=34	n=25	0.008
≤20mm	24 (70.58%)	9 (36%)	
>20mm	10 (29.42%)	16 (64%)	
Tumour size on imaging (TNBC)	n=14	n=9	0.002
≤20mm	12 (85.71%)	2 (22.22%)	
>20mm	2 (14.29%)	7 (77.78%)	
Lymph node size on imaging	n=28	n=16	0.086
≤15mm	18 (64.29%)	6 (37.5%)	
>15mm	10 (35.71%)	10 (62.5%)	
Lymph node size on imaging (TNBC)	n=11	n=7	0.914
≤15mm	5 (45.45%)	3 (42.86%)	
>15mm	6 (54.55%)	4 (57.14%)	
Tumour ≤20mm and lymph node ≤15mm	n=18	n=6	0.017
Number of abnormal lymph nodes on axillary ultrasound	n=34	n=25	0.177
1	33 (97.06%)	20 (80%)	
>1	1 (2.94%)	5 (20%)	