REVIEW ARTICLE

Role of Ultrasound in Pretreatment Evaluation of Lymph Node Status in Carcinoma Breast: A Systematic Review

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Abstract

Aim: This systematic review aimed to analyze efficacy of axillary ultrasonography (USG) in differentiating normal from abnormal lymph nodes (LNs) in breast cancer patients, taking into account the different criteria used.

Background: Identification of pretreatment axillary LN metastasis is one of the most important prognostic factors in breast cancer, and it affects the surgical plan and oncological management after surgery.

Review results: A PubMed search was made using the following items: "Ultrasonography" [Mesh] AND "Axilla" [Mesh] AND "Breast Neoplasms" [Mesh]. A total of 34 studies were included in the review analysis. Studies were divided according to the LN feature studied into six subheadings which include size, cortex thickness, hilum changes, long axis-to-short axis ratio (L/S ratio), combination of multiple morphological factors, and combination of both morphology and size. For LN size, *sensitivity* and *specificity* ranged from 49 to 95%, 34 to 97.4%; cortical thickness 35 to 96%, 36 to 92%; hilar changes 24 to 92%, 23 to 100%; L/S ratio 65 to 100%, 18 to 65%; morphological features 26 to 94%, 76 to 100%; and combination of both morphological and size 18 to 100%, 50 to 100%, respectively.

Conclusion: Role of USG in pretreatment axillary staging has been extensively studied. Various diagnostic criteria have been used for defining abnormal LN, which leads to difficult comparisons between various studies.

Clinical significance: Pretreatment evaluation of axilla with USG, using *multiple criteria,* like LN size, L/S ratio, cortical, and hilar abnormalities in combination with morphological features, gave the best accuracy for detection of abnormal nodes and lowest false-negative rates in breast cancer patients.

Keywords: Axilla, Breast neoplasm, Lymph node metastasis, Sensitivity, Specificity, Systematic review, Ultrasonography.

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Background

Carcinoma breast is the most common malignancy in females and second most common malignancy overall in the world, with the incidence of 25.8 per lakh female population and mortality rate of 12.7 per lakh population.[1] Identification of pretreatment axillary lymph node (LN) metastasis is one of the most important prognostic factors in breast cancer, and it affects the surgical plan and oncological management after surgery. Patients with carcinoma breast with LN metastasis have 4–5 times more incidence of mortality in comparison with negative nodal disease patients.[2] Historically, complete axillary lymph node dissection (ALND) was a standard for LN staging in carcinoma breast. Recently, sentinel lymph node biopsy (SLNB), which is a less invasive procedure, has become a standard procedure for axillary staging in clinically node negative, early breast cancer.[3] Also, it has been identified in American College of Surgeons Oncology Group (ACOSOG) Z0011 trial that patients with low burden of axillary disease, with node positivity detected by SLNB, have similar recurrence and overall survival when treated with either ALND or whole breast irradiation with systemic chemotherapy.[4] The limitations of SLNB are requirement of frozen section facilities, prolonged operative time, and 5–10% false negativity rate. This highlights the importance of a prediction test for axillary nodal status without any surgical intervention with a good sensitivity and low false-negative rate.

Pretreatment axillary ultrasonography (USG) is a modality for evaluation of the axillary LNs, and in conjunction with fine needle aspiration cytology, malignant LN can be confirmed to spare an unnecessary SLNB and proceed directly to ALND if needed.[5] Although ALND carries its disadvantages, like additional demands on resources, chronic nerve pain, and lymphedema, it is less morbid than two procedures (SLNB and ALND).[6] In USG axilla, multiple morphological and dimensional criteria have been evaluated to differentiate between the benign and malignant nodes, and these differ among different institutions and studies. In this review article, we aim to analyze the efficacy of axillary USG to differentiate between normal and abnormal LNs, taking into account the different criteria used.

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Methods

A literature review was performed using electronic search on Google Scholar and PubMed from 1980 to 2020. The research questions addressed were as follows:

- What is sensitivity, specificity, and accuracy of USG axilla as a screening tool for nodal metastasis in carcinoma breast?
- What are the various USG nodal features (dimensional and morphological) used to differentiate between normal and abnormal LNs?
- What is sensitivity, specificity, and accuracy of the various USG features for nodal metastasis in carcinoma breast?

Study Selection

A PubMed search was made using the following items: "Ultrasonography" [Mesh] AND "Axilla" [Mesh] AND "Breast Neoplasms" [Mesh]. The selection was limited to articles written in English only. Then, a manual analysis of the reference list of the relevant articles which were previously selected was done, and more articles were selected. The following inclusion and the exclusion criteria were used to screen the articles:

Inclusion Criteria

- Original research articles irrespective of type of design, selection of patient group, blinding, and frequency of USG machines.
- Studies that enrolled patients with breast cancer and axillary USG were performed before axillary ALND or SLNB.
- Studies using cytology or histopathology of axillary LNs as gold standard.
- Studies using size and morphological changes as relevant features in USG for axillary metastasis.

Exclusion Criteria

- Studies which included postoperative patients, patients on chemotherapy or radiotherapy, and those with prior axillary intervention.
- Studies not using cytology or histopathology of axillary LNs as gold standard.
- Full text not available during search.
- Lack of key data.
- Systematic review articles and meta-analysis articles.

After removing all the duplicate records, meticulous search of the full-text articles which gave information about the diagnostic accuracy of axillary USG in detecting LN metastasis in carcinoma breast, 34 articles were selected for this review (Flowchart 1). All studies were systematically analyzed for the type of study design, total number of subjects included, gold standard (cytology or histopathology), disease stage of population, ultrasound characteristics for detection of abnormal (involved) LN metastasis (size, morphological features, like loss of fatty hilum, hilar echotexture changes, hilar vascularity changes, long axis-to-short axis ratio or short axis-to-long axis ratio, cortex thickening, change in shape or heterogeneous node), and statistical analysis of the previously mentioned parameters alone or in combination, in terms of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Review Results

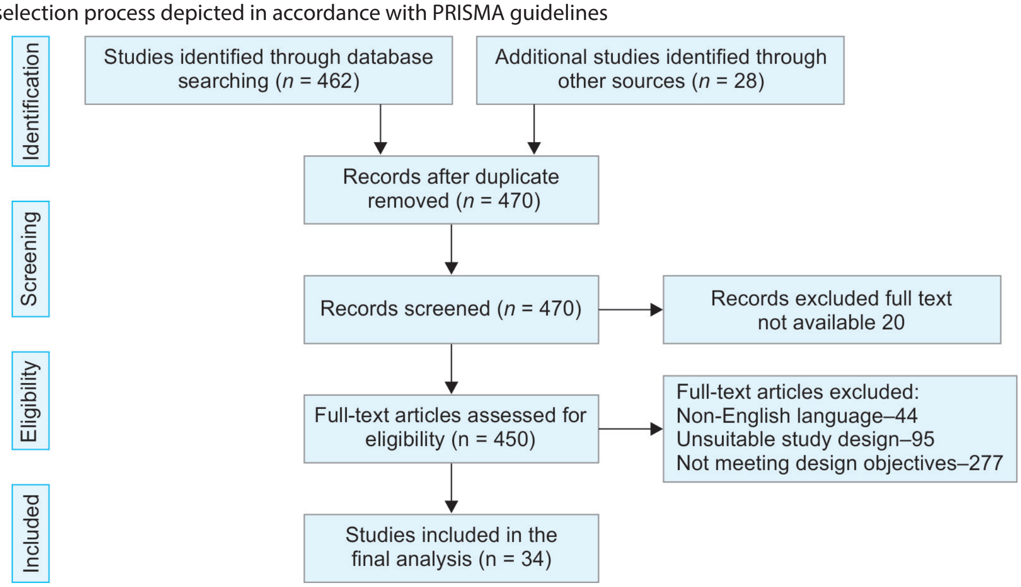
A total of 34 studies were included in the review analysis. Studies were divided according to the LN feature studied into six subheadings which include size, cortex thickness, hilum changes, long axis-to-short axis ratio (L/S ratio), combination of multiple morphological factors, and combination of both morphological and size.

Accuracy of Size of LN in Detecting Nodal Metastases

Size was one of the important criteria for detection of axillary metastasis in breast cancer. In the analyzed literature, eight studies used size as criteria for axillary metastasis (Table 1). In five studies, size more than 5 mm was taken as the criteria for positivity, the sensitivity ranged from 48.8 to 87%, and specificity from 56 to 97.4%.

In study done by Bruneton et al. in 1986 on 60 patients with all stages of carcinoma breast to evaluate the significance of USG over clinical examination with 5 mm node as cutoff criteria, they found a sensitivity of 72.7% and specificity of 97.4%. Near similar data were published by other authors using the same criteria all having final histopathology as a gold standard.[7–11] In 2009, a study done in Korea by Choi et al. on 425 patients used length more than 9.4 mm as positivity criteria gave a higher sensitivity, but lower specificity (sensitivity 83.7%, specificity 34.3%, PPV 53%, NPV 70.4%).[12] Kusum et al. published a similar study in 2018, using USG-guided cytology as gold standard, with LN size cutoff of 1.5 cm or more as a diagnostic criterion. They found the sensitivity of 77.3%, the specificity of 54.54%,

Flowchart 1: Studies selection process depicted in accordance with PRISMA guidelines



PPV of 80.4%, and NPV of 50%.[13] Choudhary et al. in 2018 used cutoff of 0.7 cm or more for diagnostic accuracy of size and found highest sensitivity of 94.8% with a specificity of 52.2%.[14]

Accuracy of Cortical Thickness of LN in Detecting Nodal Metastases

Cortical changes in the LN are indicative of tumor infiltration and useful for identifying early metastatic nodes. A total of nine studies were included in the analysis (Table 2). Two studies[11,15] used cortical thickness of 2.3 mm as cutoff value to consider it as a metastatic node, four studies[12,13,16,17] used 3 mm, one study used 3.8 mm,[18] and one study used 4 mm.[19] Bedi et al. did not use cortical thickness as criteria but used eccentric cortical lobulations as a marker of metastasis.[20]

In 2003, Deurloo et al.[11] published a study analyzing cortical thickness with a cutoff of 2.3 mm in Netherlands with 268 patients and found sensitivity of 95% and specificity of 44%. Contradictory to this, a study in 2005[15] with 732 patients and same cutoff found a lower sensitivity of 35% and higher specificity of 82%. Bedi et al.[20] in 2008 did a similar analysis; however, LN cortex was classified as one of six types according to the USG features, ranging from benign to highly hypoechoic cortical lobulations (which were classified as malignant). They found a sensitivity of 77% and specificity of 80% on 171 patients. Four studies used cortical thickness of 3 mm as cutoff for LN metastasis, out of these three used histopathology as gold standard and one used cytology as gold standard.[12,13,16,17] These were published in years 2009, 2012, 2015, and 2018, and studied a total of 643 patients. The sensitivity in these studies ranged from 66.7 to 96.6% and specificity from 12.5 to 74.5%. Lee et al.[18] used a cutoff of 3.8 mm on 105 patients and found a low sensitivity (56.34%) and highest specificity (92.31%). A study published in 2009[19] enrolled 144 patients with cutoff of 4 mm, and found the sensitivity and specificity to be 88 and 42%, respectively.

Accuracy of Hilar Changes of LN in Detecting Nodal Metastases

Only six studies had analyzed LN on the basis of hilar changes, and all were published in the year 2009 and later (Table 3). The criteria taken into account were presence and absence of hilum, changes in echogenicity of hilum, and assessment of hilar blood flow on Doppler study. Five studies used histopathology as a gold standard whereas

Table 1: Results of studies that used LN size as diagnostic criteria for nodal metastasis in carcinoma breast

Sl. No.	Study	Year	Gold standard	Criteria	N	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	Bruneton et al.[7]	1986	ALND	Size >5 mm	60	72.7	97.4	NR	NR
2	Tate et al.[8]	1989	ALND	Size >5 mm	140	66.1	75.3	NR	NR
3	Vaidya et al.[9]	1996	ALND	Size >5 mm	200	69	90	90	69
4	Bonnema et al.[10]	1997	ALND	Size >5 mm	150	87	56	58	86
5	Deurloo et al.[11]	2003	ALND	Size >5 mm	268	48.8	76.9	NR	NR
6	Choi et al.[12]	2009	ALND	Size >9.4 mm	425	83.7	34.3	53	70.4
7	Kapila et al.[13]	2018	FNAC	Size >15 mm	75	77.3	54.54	80.39	50
8	Choudhary et al.[14]	2018	ALND	Size >7 mm	62	94.8	52.17	77.08	85.7

ALND, axillary lymph node dissection; FNAC, fine needle aspiration cytology; PPV, positive predictive value; NPV, negative predictive value

Table 2: Results of studies that used cortical changes as diagnostic criteria for nodal metastasis in carcinoma breast

Sl. No.	Study	Year	Gold standard	Criteria	N	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	Deurloo et al.[11]	2003	ALND	Cortex thickness >2.3 mm	268	95	44	NA	NA
2	Van Rijk et al.[15]	2006	ALND	Cortex thickness >2.3 mm	732	35	82	53.4	68.2
3	Bedi et al.[20]	2008	ALND	Cortex lobulations	171	77	80	36	96
4	Choi et al.[12]	2009	ALND	Cortex thickness >3 mm	425	68.8	72.9	68.8	71.6
5	Abe et al.[19]	2009	ALND	Cortex thickness >4 mm	144	88	42	73	71
6	Oz et al.[16]	2012	ALND	Cortex thickness >3 mm	38	96.6	12.5	80.5	50
7	Lee et al.[18]	2013	ALND	Cortex thickness >3.8 mm	224	56.34	92.31	93	53
8	Stachs et al.[17]	2015	ALND	Cortex thickness >3 mm	105	66.7	74.6	63.6	77
9	Kapila et al.[13]	2018	FNAC	Cortex thickness >3 mm	75	94.34	36.36	78.13	72.72

ALND, axillary lymph node dissection; FNAC, fine needle aspiration cytology; PPV, positive predictive value; NPV, negative predictive value

Table 3: Results of studies that used hilar changes as diagnostic criteria for nodal metastasis in carcinoma breast

Sl. No.	Study	Year	Gold standard	Criteria	N	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1	Choi et al.[12]	2009	ALND	Presence/absence hilum	425	24.5	94.6	80	58.6
2	Abe et al.[19]	2009	ALND	Presence/absence hilum	144	33	97	93	53
3	Oz et al.[16]	2012	ALND	Hilar changes, nonhilar flow	38	33.3	100	100	23.7
4	Lee et al.[18]	2013	ALND	Hilum echotexture changes	224	40.8	92.3	90	46
5	Kapila et al.[13]	2018	FNAC	Altered hilar echotexture	75	92.45	23.44	87.5	78.95
6	Choudhary et al.[14]	2018	ALND	Hilar blood flow changes	62	79.49	95.65	96.87	73.33

ALND, axillary lymph node dissection; FNAC, fine needle aspiration cytology; PPV, positive predictive value; NPV, negative predictive value only one study used cytology. Chio et al. in 2009 used presence and absence of hilum as criterion for axillary metastasis on 425 patients and found a low sensitivity of 24.5% and high specificity of 94.6%.[12] Study done by Hiroyuki Abe et al. found similar results.[19] In 2012, study was done using hilar blood flow and hilar fat changes as criteria in 38 patients and found 100% specificity but a low sensitivity of 33%.[16] In 2013, a study done by Belinda Lee et al. found slightly better sensitivity of 40.8%.[18] In contrast, in 2018, Kapila et al. used altered hilar echotexture and found the highest sensitivity of 92.45% with a low specificity of 23.44%.[13] Study published by Chaudhary et al. in 2018 used high-resolution USG and color Doppler, and found that hilar blood flow changes had sensitivity of 79.49%, specificity of 95.655, PPV of 96.87, and NPV of 73.33%.[14]

Accuracy of L/S of LN in Detecting Nodal Metastases

Benign nodes are more likely to be ovoid, and they become more rounded as a result of malignant infiltration. Historically, a ratio of long axis to short axis (L/S ratio) less than 2 is considered to be significant for malignancy. Only five published articles evaluated L/S ratio for detection of metastatic axillary LNs (Table 4). Four studies used L/S ratio <2 as the cutoff criteria, and one study used criteria as short axis-to-long axis ratio (S/L ratio) >0.35.

In the four studies that used L/S ratio <2 as the cutoff, a total of 600 patients were enrolled, the sensitivity ranged from 65.3 to 100%, and specificity from 18.18 to 65.22%.[12–14,16] Lee et al.[18] published an article in 2013, using the criteria of S/L ratio >0.35 on 224 patients, and found a sensitivity of 90.1% and specificity of 33.3%.

Accuracy of Morphological Features of LN in Detecting Nodal Metastases

Morphological nodal parameters are one of the key features central to accurate nodal staging in carcinoma breast. All studies which used conjunction of multiple morphological features to evaluate for axillary metastasis were included. In the analyzed literature, 17 studies used a combination of morphological features for identifying the suspicious LN (Table 5). The LN factors which were analyzed were shape, echogenicity, hilum or cortical changes, and altered vascular flows. Most of the studies used histopathology as a gold standard except single study done by Sapino et al.[5,24] which used cytology as a gold standard. The sensitivity raged between

Table 4: Results of studies that used L/S ratio as diagnostic criteria for nodal metastasis in carcinoma breast

Sl. No.	*Study*	*Year*	*Gold standard*	*Criteria*	*N*	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*
1	Choi et al.[12]	2009	ALND	L/S ratio <2	425	65.3	52.4	54.9	63
2	Oz et al.[16]	2012	ALND	L/S ratio <2	38	100	37.5	85.7	100
3	Lee et al.[18]	2013	ALND	S/L ratio >0.35	224	90.1	33.3	71	65
4	Kapila et al.[13]	2018	FNAC	L/S ratio <2	75	67.92	18.18	66.67	17.39
5	Choudhary et al.[14]	2018	ALND	L/S ratio <2	62	79.49	65.22	79.49	65.22

ALND, axillary lymph node dissection; FNAC, fine needle aspiration cytology; L/S, long/short axis; S/L, short/long axis; PPV, positive predictive value; NPV, negative predictive value

Table 5: Results of studies that used morphological features as diagnostic criteria for nodal metastasis in carcinoma breast

Sl. No.	*Study*	*Year*	*Gold standard*	*Criteria*	*N*	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*
1	Lam et al.[21]	1996	ALND	Hypoechoic node, hilum changes, cortical hypertrophy	36	72.7	95	NA	NA
2	Yang et al.[22]	1996	ALND	Round node, cortical thickness, and obliteration of hilum	114	84.1	97.1	94.9	90.7
3	Bonnema et al.[10]	1997	ALND	Hypoechoic, heterogeneous node	150	36	95	86	63
4	Yang et al.[23]	1998	ALND	Loss of hilum, eccentric cortical hypertrophy	81	79.5	94	91.2	85.5
5	Sapino et al.[24]	2003	FNAC	Round, echopoor central hilum, and eccentric cortex	267	63.6	75.8	51.6	83.7
6	Bedrosian et al.[25]	2003	ALND	Eccentric cortical enlargement with displacement of fatty hilum	144	26.4	91	50	78.3
7	Mobbs et al.[26]	2005	ALND	Change of shape, loss of the central fatty hilum, thickened cortex	71	40	82	47	78
8	Nathanson et al.[27]	2007	ALND	Round shape, eccentric cortex, focal bulging of the cortex, displacement or obliteration of the hilum	179	77.3	94.4	94.4	77.3
9	Abe et al.[19]	2009	ALND	Cortical thickening and nonhilar blood flow	144	65	81	81	65
10	Mainiero et al.[28]	2010	ALND	Focally thickened cortex ≥3 mm or the fatty hilum was absent	224	59	100	NA	NA
11	Torres Sousa et al.[29]	2011	ALND	Cortical thickness ≥3 mm, obliteration or eccentric location of the hilar fat, nonhilar cortical blood flow	197	94	NA	100	88.9

12	Park et al.[30]	2011	ALND	Loss of fat hilum, cortical thickening of more than 3 mm, irregular shape, round shape, or increased nonhilar flow	382	56.3	81	60.3	78.5
13	Valente et al.[31]	2012	ALND	Rounded, a long-to-short axis ratio of <2, hypoechoic, disappearance of the fatty hilum, or cortical thickening	244	43.5	96.2	79.3	83.3
14	Lee et al.[18]	2013	ALND	S/L ratio >0.35, cortex thickness >3.8 mm, altered hilum echotexture	224	53.7	85.1	81.5	60.5
15	Farrell et al.[32]	2015	ALND	Cortical thickness >3 mm, prominent eccentric lobulations, and a replaced/eccentric hilum	679	64	76.9	63.8	77.1
16	Stachs et al.[17]	2015	ALND	L/S ratio <2, hypoechoic hilum, thickened cortex	105	45.2	87.3	70.5	70.4
17	Dihge et al.[33]	2016	ALND	Cortical thickening, absence of a fatty hilum, and altered shape	473	23	95	73	68

ALND, axillary lymph node dissection; FNAC, fine needle aspiration cytology; L/S, long/short axis; S/L, short/long axis; PPV, positive predictive value; NPV, negative predictive value

Table 6: Results of studies that used combination of morphology and size of LN as diagnostic criteria for nodal metastasis in carcinoma breast

Sl. No.	*Study*	*Year*	*Gold standard*	*Criteria*	*N*	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*
1	Oruwari et al.[34]	2002	ALND	Size >1 cm, loss of a fatty hilum, and a hypoechoic parenchyma	27	91	100	NR	NR
2	Damera et al.[35]	2003	ALND	L/S <2, cortex eccentrically thickened to more than 2 mm	166	55	82	74	65
3	Shetty et al.[36]	2004	ALND	Size greater than 20 mm, absence of a fatty hilum, abnormal cortex	20	100	50	50	100
4	Kebudi et al.[37]	2005	ALND	Centric echogenicity, thickening of cortex, length/width ratio (L/W), and the diameter of LNs	42	79.1	77.7	82.6	73.6
5	Cowher et al.[38]	2008	ALND	Enlarged, hypoechoic, enlarged cortex, and loss of architecture	152	18.52	96.36	71.4	70.6
6	Abe et al.[19]	2009	ALND	Cortical, hilum, and size changes	144	84	53	69	72
7	Cools-Lartigue et al.[39]	2013	ALND	Absence of a fatty hilum, eccentric cortical thickening, and a round hypoechoic node (>1 cm)	235	55	88	74	75
8	Ertan et al.[40]	2013	ALND	LNs' size 2 cm in diameter, L/S >2, loss of central echo, increased intranodal vascularization	172	58	91.6	80	73

ALND, axillary lymph node dissection; FNAC, fine needle aspiration cytology; L/S, long/short axis; S/L, short/long axis; PPV, positive predictive value; NPV, negative predictive value

23 and 94%, specificity ranged from 75 to 100%, PPV ranged from 47 to 100%, and NPV ranged from 60.5 to 90.7%.

In the studies published in 1990s on 381 patients, sensitivity and specificity ranged from 36 to 84.1% and 94 to 97.1%, respectively; in the years 2000 to 2010 on 1,029 patients, sensitivity and specificity ranged from 26.4 to 77.3% and 75.8 to 100%, respectively; and in the years 2011 to 2020 on 2,324 patients, sensitivity and specificity ranged from 23 to 94% and 76.9 to 96.2%, respectively.

Accuracy of Combination of Both Morphology and Size of LN in Detecting Nodal Metastases

Out of 34 studies, 8 studies had used conjunction of both dimensional and morphological features of LN for suspicion of metastatic LNs with histopathology as the gold standard criteria (Table 6). A variable sensitivity ranging from 18 to 100% and specificity ranging from 50 to 100% was found. Oruwari et al.[1] in year 2002 showed highest sensitivity of 91% and specificity of 100%, but the limitation of the study was sample size of only 27 patients. Colls-Lartigue et al.[7] had the largest sample size of 235 patients; they used diagnostic criteria of absence of fatty hilum, eccentric cortical thickening, and a round hypoechoic node of >1 cm. In this study, the sensitivity and the specificity were 55 and 88%, respectively. Highest sensitivity (100%) was achieved with the following LN criteria—size greater than 20 mm, absence of a fatty hilum, abnormal cortex,[4] highest specificity (100%) with size >1 cm, loss of a fatty hilum, and a hypoechoic parenchyma.[1]

Discussion

Pretreatment staging of axilla using palpation, USG, or SLNB/ALND is essential in carcinoma breast patients. A wide range of sensitivity and specificity had been reported by authors, using a range of descriptors for the axillary USG. Role of USG in pretreatment axillary staging has been extensively studied, and various diagnostic criteria have been used for defining the criteria which leads to difficult comparisons.

Size is one of the earliest criteria which was used to suspect a LN with metastasis because length assessment was easily possible with a low-frequency machine. But, it has been identified that size alone cannot be used as relevant criteria, as metastatic nodes may be small and acute inflammatory or reactive nodes may be quite large which can be seen as poor specificity of size as a marker of metastatic LN.[41] In the literature, the clinical palpation of LN was associated with high false-negative rate of 32% and false-positive rate of 26%; a similar result was found for USG, as the mean specificity for size as a criteria for axillary metastasis was only 67%.[42] In this literature review, we found that a LN size cutoff of >5 mm had higher specificity than sensitivity, as this cutoff was raised to >7, 9.5, or 1.5 mm, the sensitivity increased, and the specificity fell.

Cortical changes are one of the earliest changes which have been described due to the physiology of lymph flow that carries the metastasis to the LN. Metastatic cells from the afferent lymphatic channels reach the cortex and paracortex first where the metastatic cells are arrested by phagocytes at the periphery of the node causing focal enlargement of the cortex (which can be localized or eccentric) and at a later stage causing generalized enlargement of the cortex and eventually the entire node.[20] Cortical abnormalities found in this review included focal or diffuse thickening of >3 mm and the presence of focal bulges of the cortex. A total of nine studies were included in the review, evaluating the accuracy of cortical thickness for the axillary metastasis. These studies utilized 2.3–4 mm cortical thickness as the criteria to detect abnormal LN, most had demonstrated a good sensitivity but low specificity, owing to changes in many of the benign conditions. It is also important to consider that cortical lobulation is a subjective feature which may lead to inter- and intraobserver variations.

Usually, in a benign LN, the hilum is hyperechogenic due to connective tissue trabeculae, lymphatic tissue cords, and medullary sinusoids. Decrease or absence of hilum, changes in shape, and vascular pattern are considered suspicious and the most specific alteration for metastatic disease.[20] Recent advances in high-resolution USG allow examination of more detailed features of LNs, like internal hilar echogenicity, which may prove to be useful indicators of metastasis.[12] In this review, all but one study have established a high specificity (92.3–100%) but a low sensitivity. This is because of the late involvement of the hilum in case of metastasis to a LN. Any change in the hilar vasculature is one of the best criteria to differentiate from a benign LN. The limitations associated with hilar changes are observer bias and need of a high-resolution Doppler ultrasound.

The shape of the LN is assessed using the L/S ratio. An L/S ratio <2 indicates a round node whereas an L/S ratio >2 indicates an oval or elongated node, also known as *Solbiati index*.[43] Most of the studies in this review have used L/S ratio, and one study has used S/L ratio >0.35. The studies showed a better sensitivity than specificity suggesting a higher false-positive rate for suspicion of metastasis in axillary LN when used alone.

Overall accuracy to detect axillary metastasis with USG substantially improved with the use of multiple morphological factors with or without conjunction of size of the LN. The various morphological features used were shape, echogenicity, hilum or cortical changes, echogenicity of hilum, and changes in vascular pattern on Doppler. Some studies demonstrated better sensitivity and others better specificity, with highest sensitivity and specificity reaching 100%.

Limitations

The major limitation of this review is that results could not be compared across the studies due to the differences in methodology. There may be multiple factors which could lead to the variability in the data, like choice of gold standard, type of patients selected, the way in which they were selected, different equipment, different transducer frequencies, and small variations existed in the criteria applied by different authors to determine on USG whether the node was benign or malignant.

Clinical Significance

Pretreatment evaluation of axilla with USG, using multiple criteria, like LN size, L/S ratio, cortical, and hilar abnormalities in combination with morphological features, gave the best accuracy for detection of abnormal nodes and lowest false-negative rates in breast cancer patients. USG axilla, when performed by a dedicated sonologist, is a valuable tool for evaluation of axillary nodes.

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