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ORIGINAL RESEARCH

Diagnostic potential of conventional ultrasonography combined with elastography in assessing the properties of axillary lymph nodes in breast cancer

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Abstract

This study was done to assess the potential of conventional ultrasound combined with ultrasound elastography (UE) for diagnosing the nature of lymph nodes in breast cancer. The study included 45 breast cancer patients who underwent axillary lymph node dissection. Routine ultrasound and UE were conducted one week before the surgery. Logistic regression analysis was used to examine the factors that influence the nature of axillary lymph nodes. It also assessed whether patients with breast cancer needed axillary lymph node dissection. Forty-five breast cancer patients underwent axillary lymph node dissection and were diagnosed by surgical pathology as 20 metastatic and 25 reactive axillary lymph nodes. Statistically significant differences from univariate analysis were found between the metastatic and reactive lymph nodes in breast cancer patients regarding length to short axis ratio (L/S), cortical thickness, lymph node grading, blood flow type, and elasticity score. Breast cancer lymph node metastases were associated with the variables included by univariate analysis into the binary logistic regression model ($p < 0.05$). Logistic regression model: Logit (p) = $-1.894 + 1.554X_1 + 0.789X_3 + 2.174X_4$. Plotting the receiver operating characteristic (ROC) curve revealed that the area under the curve (AUC) of the regression model for diagnosing metastatic lymph nodes in breast cancer was: 0.880, 95% Confidence Interval (0.783–0.977), and the performance was good.

Keywords

Breast cancer; Lymph nodes; Conventional ultrasound; Ultrasound elastography; Application value

1. Introduction

The primary site of breast cancer metastasis occurs in axillary lymph nodes. Modified radical surgery includes axillary lymph node dissection as the traditional effective treatment [1–4]. Many breast tumors are discovered for the first time without axillary lymph node metastases. The phenomenon can be attributed to increasing health awareness and conducting physical examinations. A blind axillary lymph node dissection may thus be an unnecessary surgery [5, 6]. The application of sentinel lymph node biopsy has largely reduced unnecessary axillary lymph node dissection, lowered the risk of postoperative upper extremity edema and activity limitation, and improved patient quality of life. However, accurate preoperative assessment of the nature of axillary lymph nodes in breast cancer is imperative in developing surgical plans for precise individualized treatment. Clinical palpation methods, X-ray mammography, CT (Computed Tomography), and magnetic resonance imaging (MRI) are the common clinical methods to determine the nature of axillary lymph nodes in breast cancer. However, they have limited clinical application potential. Ultrasound is the common imaging method used to clinically diagnose breast cancer. It reveals changes in lymph nodes through morphology, length-to-short axis ratio, and blood flow type [7–9]. Conversely, ultrasound elastography (UE) reflects tissue texture and hardness for the assessment and clinical identification of lymph node characteristics [10–12]. The following study is conducted to investigate the potential of conventional ultrasound combined with UE to identify the nature of axillary lymph nodes in breast cancer.

2. Object and method

2.1 Study subjects

Forty-five breast cancer patients with axillary lymph node dissection having been admitted to the hospital were included in the study. (1) Inclusion criteria: ipsilateral axillary lymph nodes with pathologically confirmed primary breast cancer; routine ultrasound and UE performed 1 week before the surgery; complete imaging data; and axillary lymph nodes with postoperative pathological findings.

(2) Exclusion criteria: other lymph node-related diseases; and where pathological specimens could not be obtained.

2.2 Methods

2.2.1 Examination instruments

HITACHI Vision Preirus ultrasound diagnostic instrument (Model HI VISION Preirus, Hitachi, Tokyo, Japan) with a high-frequency line array probe and probe frequency of 7~10 MHz was utilized.

2.2.2 Examination method

(1) Preparation before examination: the patient laid down in a supine position with both upper limbs raised and abducted. The bilateral mammary glands and axillae were repeatedly exposed. (2) Conventional ultrasound was performed: suspicious axillary lymph nodes were selected to measure lymph node long axis, short axis, and cortical thickness in the long-axis section. The lymph node aspect ratio was calculated. They were scanned in multiple sections. Their morphology and blood flow status were observed. Blood flow grading and the type were recorded. (3) UE examination was performed: the lymph node long-axis section was selected to start the dual-amplitude elastography mode (UE). The region of interest (ROI) range was adjusted. The probe was held perpendicular to the axillary lymph node direction. The pressure index was kept between 3–4 with continuous pressure. The lymph node elastography score was measured according to Choi JJ's four-point method.

2.2.3 Ultrasound image analysis

The two-dimensional ultrasound characteristics were assessed: an aspect ratio of <2 was defined as the metastatic lymph node and graded as 3–5. Lymph nodes were classified into 5 grades according to the cortical thickness, and presence or absence of lymph node portal structures.

Blood flow grading: the semi-quantitative blood flow grading criteria of Adler *et al*. [13] were used to divide into 0, 1, 2 and 3 grades, where grades 0–1 were the non-metastatic and 2–3 were the metastatic lymph nodes.

The lymph node blood flow types were classified as no blood flow, portal, peripheral, and mixed. Peripheral and mixed blood flow types were considered as the metastatic lymph nodes.

Elasticity scoring criteria: elasticity scoring was made using the 4-point method of "Choi JJ" [14], where elasticity scores of 1 to 2 were diagnosed as the non-metastatic and 3–4 as the metastatic lymph nodes.

2.3 Statistical methods

The data processing was made by Statistical Package for The Social Sciences (SPSS) version 22 (produced by BMI, Inc., Chicago, IL, USA). Count data were expressed as examples. Chi-squared (χ^2) test was performed, and the variables from statistically significant univariate analysis were subjected to multi-factor logistic regression analysis. Variables were screened using the backward method. Receiver operating characteristics (ROC) curves were plotted to evaluate the diagnostic efficacy of the prediction model for metastatic lymph nodes in breast cancer. $p < 0.05$ was considered a statistically significant difference.

3. Results

3.1 Pathological results analysis

The surgical pathology of 45 breast cancer patients who underwent axillary lymph node dissection revealed 20 metastatic and 25 reactive axillary lymph nodes.

3.2 Ultrasound analysis of metastatic and reactive lymph nodes by factors

Univariate analysis depicted statistically significant differences ($p < 0.05$) between reactive and metastatic lymph nodes in breast cancer regarding L/S, cortical thickness, lymph node grading, blood flow type, and elasticity score (Table 1).

3.3 Multifactorial regression analysis of ultrasound parameters

The indicators significant for univariate analysis were included in the binary logistic regression model (Table 2 for assignment instructions). The analysis in Table 3 suggested a significant relationship between L/S, blood flow type, elasticity score, and lymph node metastasis in breast cancer ($p < 0.05$). Logistic regression model: Logit $(p) = -1.894 + 1.554X_1 + 0.789X_3 + 2.174X_4$.

3.4 Logistic regression model potential in identifying the nature of lymph nodes in breast cancer

Plotting the ROC curve revealed that the area under the curve (AUC) of the regression model for diagnosing metastatic lymph nodes in breast cancer was: 0.880, 95% CI (0.783–0.977), suggesting good performance as shown in Fig. 1.

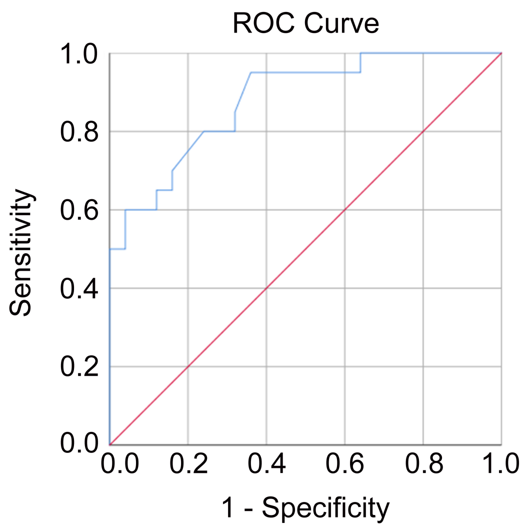

FIGURE 1. Potential of a logistic regression model based on conventional ultrasound and UE for diagnosing the nature of lymph nodes in breast cancer. ROC: receiver operating characteristic.

TABLE 1. Ultrasound analysis results of metastatic versus reactive lymph nodes for each factor (cases).

Ultrasound parameters	Grouping	Metastatic lymph nodes (n = 20)	Reactive lymph nodes (n = 25)	χ^2	p
L/S					
	<2	10	4	5.993	0.014
	≥2	10	21		
Morphology					
	Rounded	7	3	3.401	0.065
	Irregular	13	22		
Cortical thickness combined with lymph node grading					
	1–2 level	2	13	8.820	0.003
	3–5 level	18	12		
Blood flow type					
	Peripheral or mixed type	11	2	11.948	<0.001
	Central type	9	23		
Blood flow classification					
	0–1 level	3	5	0.190	0.663
	2–3 level	17	20		
Elasticity score					
	1–2 points	5	17	8.222	0.004
	3–4 points	15	8		

L/S: length to short axis ratio.

TABLE 2. Assignment description.

Variables	Variable name	Assignment description
Nature of lymph nodes	Y	Reactive lymph nodes = 0, Metastatic lymph nodes = 1
L/S	X_1	≥2 = 0, <2 = 1
Cortical thickness and lymph node grading	X_2	1–2 level = 0, 3–5 level = 1
Blood flow type	X_3	0–1 level = 0, 2–3 level = 1
Elasticity score	X_4	1–2 points = 0, 3–4 points = 1

L/S: length to short axis ratio.

TABLE 3. Multi-factor regression analysis of ultrasound parameters affecting the nature of lymph nodes in breast cancer.

Factor	β	SE	Wald χ^2 value	OR	p	95% CI
L/S	1.554	0.698	4.957	4.730	0.027	1.204–18.580
Cortical thickness and lymph node grading	1.151	0.590	3.806	3.161	0.052	0.995–10.048
Blood flow type	0.789	0.116	46.263	2.201	<0.001	1.754–2.763
Elasticity score	2.174	0.877	6.145	8.793	0.014	1.576–49.054

L/S: length to short axis ratio; SE: Regression Coefficient; OR: Odds Ratio; CI: Confidence Interval.

4. Discussion

A preoperative assessment of the type of axillary lymph nodes was important for making a clinical choice to undertake axillary lymph node dissection. The majority of reactive lymph nodes in conventional ultrasound had an oval shape, aspect ratio of >2, intact and smooth periphery, were homogeneously hypoechoic in cortical area, and exhibited short-rod blood flow signal with color Doppler [15–18]. Cancer cells continued proliferation where some of the cortices of metastatic lymph nodes depicted uneven thickness, and portal structures were damaged, resulting in morphological alterations. Metastatic lymph nodes were mainly circular and the L/S ratio was lower in conventional ultrasonography. The hypoechoic cortical regions were irregularly thickened [19, 20]. In this study, 50% of 20 metastatic lymph nodes diagnosed by pathological examination had a conventional ultrasound L/S ratio of <2, while the proportion was only 16% in reactive lymph nodes. The conventional ultrasound cortical thickness and lymph node portal structure of metastatic lymph nodes were graded as 3–5, while reactive lymph nodes as 1–2.

In the early stage of breast cancer lymph node metastasis, the cortical part is the first to be invaded. The cancer cells can stimulate the formation of neovascularization. The distribution of blood flow in the marginal part of the cortex increases, which is favorable for the growth and metastasis of the cancer cells in the cortical part so that the internal blood flow of the lymph node manifests as a peripheral type [21–23]. In contrast, the reactive lymph nodes were more common with the central type of blood flow distribution. Therefore, the blood flow type of lymph nodes had value in identifying the nature of axillary lymph nodes. In the present study, 55% of metastatic lymph nodes had peripheral or mixed type of blood flow, while the reactive lymph nodes had the central type. Since the reactive lymph nodes remained rich in internal blood flow when combined with inflammatory reactions, the blood flow grading in lymph nodes was of little value in distinguishing the nature of lymph nodes [24–27].

UE can reflect the texture and hardness of tissues. Due to the invasion of cancer cells, the tissue structure of metastatic lymph nodes changes, and the hardness of lymph nodes increases. Due to the infinite proliferation of cancer cells, they can rapidly proliferate in lymph nodes and fill up the lymph nodes, resulting in increased cell density in lymph nodes, increased tension in lymph nodes, swelling, and hardening of lymph nodes, which is shown as blue color in UE. As the disease continues to develop, the cancer cells break through the peripheral membrane of lymph nodes and adhere with the surrounding tissues, resulting in weakening of the mobility of lymph nodes, further increasing hardness, and the range of blue color in UE will be further enlarged [28–30]. Elasticity score could thus accurately assess the structural characteristics of lymph nodes.

In this study, the binary logistic regression analysis suggested a relationship of L/S, blood flow type, and elasticity score, with breast cancer lymph node metastasis. The characteristics of axillary lymph nodes in breast cancer were used as the dependent variables, and standard ultrasound parameters of lymph nodes and elastography parameters L/S, cortical thickness combined with lymph node portal grading, blood flow type, and elasticity score as the independent variables. Logistic regression model: $\text{Logit}(p) = -1.894 + 1.554X_1 + 0.789X_3 + 2.174X_4$. Plotting the ROC curve revealed that the AUC of the regression model in diagnosing metastatic lymph nodes in breast cancer was: 0.880, 95% CI (0.783–0.977), suggesting good potential of combined conventional ultrasound and UE in identifying the nature of lymph nodes.

5. Conclusions

In conclusion, there was a significant relationship between L/S, blood flow type, elasticity score, and metastatic lymph nodes in breast cancer. The combined conventional ultrasound and UE performed well in identifying the nature of lymph nodes.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

YBC, JC—designed the study and carried them out; YBC, JC, NC, JJQ, XLL and CYX—supervised the data collection, analyzed the data, interpreted the data, prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Nanjing First Hospital (Approval no. KY20230615-02-ks-01). Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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