Cohort Study

ANNALS OF MEDICINE & SURGERY

OPEN

Prediction of axillary lymph node metastasis using tumor volume to breast volume ratio: retrospective cohort study

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Background: Tumour size appear to be a risk factor of axillary lymph node metastasis in breast cancer. Recent evidence shows that higher the T staging is associated with higher rate of axillary lymph node metastasis. However, no studies shows that in the same T staging or tumour size but different breast size or breast volume the incidence of axillary lymph node metastasis differ or not .
Objectives: This Study aimed to investigate the association between tumour to breast ratio in breast cancer as a predictive factor of axillary lymph node metastasis
Methods: This study included 200 consecutive patients diagnosed with breast cancer between January 2012 to march 2022. The authors retrospectively reviewed medical data pathologic report and Ultrasonography and mammography of breast. Tumour diameter reported in pathologic report was used to calculate tumour volume using formula for ellipse. Breast volume was calculate using formula referencing from study of *Jack W. Rostas et* all by formula Breast Volume = 1/3 × ¶ × Radius^{2}ccview × Heightccview by measuring from mammography of patient. Tumour volume to breast volume ratio was calculated and analyzed
Result: Of 200 patient included in this study, 84 patient (42%) was in lymph node positive group and 116 patient (58%) was in lymph node-negative group. Median for tumour and breast volume ratio in node positive group was higher [median 0.0093 (interquartile range = 0.0047–0.023)] than in node-negative group [median 0.0065 (interquartile range (0.0028–0.0199)]. $P = 0.0414$ receiver operating characteristic curve for tumour to breast ratio showed AUC of 0.7389 (95% CI 0.67993–0.82335) Which seems to be a significance as predictive factors for Axillary lymph node metastasis
Conclusion: Higher tumour volume to breast volume ratio tends to be a significance predictive factors for axillary lymph node metastasis in breast cancer patients

Keywords: axillary lymph node metastasis, prediction, tumour to breast ratio

Introduction

Tumour size and T staging have been identified as risk factors for axillary lymph node metastasis in previous studies[1]. However, there is limited research on whether breast size or volume influences the incidence of axillary lymph node metastasis, particularly for cases with the same T staging or tumour size[2,3].

The objective of this study is to investigate the association between the ttuom to or#atto#breast ratio in breast cancer and its potential as a predictive factor for axillary lymph node metastasis. By examining the relationship between the ttuom to tumor-to-breast ratio and axillary lymph node metastasis, the study aims to determine if breast size or volume contributes to the likelihood of lymph node involvement, independent of tumour size or T staging. The findings of this study will provide valuable insights into the role of breast size in predicting axillary lymph node metastasis in breast cancer patients with similar tumour characteristics.

HIGHLIGHT

- Higher tumour volume to breast volume ratio indicating a more aggressive disease that is more likely to spread to the lymph nodes.
- Higher ratio may indicate a greater tumour burden relative to the size of the breast.
- Multivariate analysis found that lymphovascular invasion was a strong associated factor with lymph node metastasis.

Material and method

The study was conducted as a retrospective review of medical records, ultrasound, and mammography findings of 200 consecutive patients who received treatment from 2019 to 2021. The

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2024) 86:69–72

Received 14 September 2023; Accepted 27 October 2023

Published online 17 November 2023

http://dx.doi.org/10.1097/MS9.0000000000001481

patients were divided into two groups: those with axillary lymph node metastasis and those without axillary lymph node metastasis.

Informed consent was obtained from all patients and the study was approved by Institutional Review Board. The protocol had been registered at Thai Clinical Trials Registry (TCTR) and this research has been reported in line with the STROCSS criteria[4].

The inclusion criteria for the study were as follows:

Patients diagnosed with breast cancer age between 18 and 80 years old.

Patients who underwent breast ultrasound and mammography.

Availability of pathological reports indicating tumour diameter in all dimensions.

The exclusion criteria were:

Patients with bilateral breast cancer or metastatic disease.

Patients with more than one breast cancer.

Demographic data were collected for all patients, including age, lymph node status, lymphovascular invasion, histologic grading, oestrogen receptor (ER) status, progesterone receptor (PR) status, human epidermal growth factor receptor 2 (HER-2) status, tumour location (quadrant), and type of surgery (mastectomy or breast-conserving surgery).

Breast mammogram images were analyzed to calculate breast volume using a formula derived from a study by Rostas and colleagues[5]. The formula used was $1/3 \times \pi \times R^2$ (cc view) $\times$ H (cc), and the results were reported in cm^3. (Fig. 1) Tumour diameter reported in the pathological report was used to calculate tumour volume using an elliptical formula. The tumour volume to breast volume ratio was then calculated and analyzed in the univariate analysis to assess its association with lymph node metastasis. In the multivariate analysis, other factors that could potentially correspond to lymph node metastasis were included.

Statistical analysis

The statistical analysis in this study was conducted using Stata statistical software version 12. The Wilcoxon rank-sum test was used to compare two independent samples, as it is suitable for non-parametric data when the distribution is skewed. The median values were used to compare between the two groups, considering the skewed distribution of the data.

To evaluate the predictive efficacy of the Tumour volume to breast volume ratio, a receiver operating characteristic (ROC) curve was constructed. The area under the ROC curve was calculated to assess the accuracy of the predictive model. The level of statistical significance was set at 0.05, indicating that a *P* value less than 0.05 was considered statistically significant.

Result

Dermographic data

Patients in the lymph node positive group accounted for 42%, while those in the lymph node-negative group accounted for 58%. There were no statistically significant differences observed in demographic data such as age, lymph node status, histologic grading, ER, PR, HER-2 status, tumour location (quadrant), and type of surgery (mastectomy or breast-conserving surgery) between the two groups. However, there was a statistically significant difference observed in lymphovascular invasion, as indicated in Table 1.

In our univariate analysis, we found that a higher tumour volume to breast volume ratio is associated with a higher incidence of axillary lymph node metastasis. The median tumour volume to breast volume ratio in the lymph node positive group was 0.0093 (interquartile range = 0.0047–0.023), while in the lymph node-negative group it was 0.0065 (interquartile range = 0.0028–0.0199). The *P* value for this association was calculated as 0.0414, indicating statistical significance. Furthermore, the area under the ROC curve was determined to be 0.7516, indicating acceptable predictive efficacy of the tumour volume to breast volume ratio in determining axillary lymph node metastasis.

In the multivariate analysis, lymphovascular invasion (LVI) was found to be a strong associated factor with lymph node metastasis. This suggests that the presence of LVI increases the likelihood of lymph node involvement. However, most of the other parameters evaluated in the study did not show statistical significance in their association with lymph node metastasis. This means that factors such as age, histologic grading, hormone receptor status (ER, PR, HER-2), tumour location (quadrant),

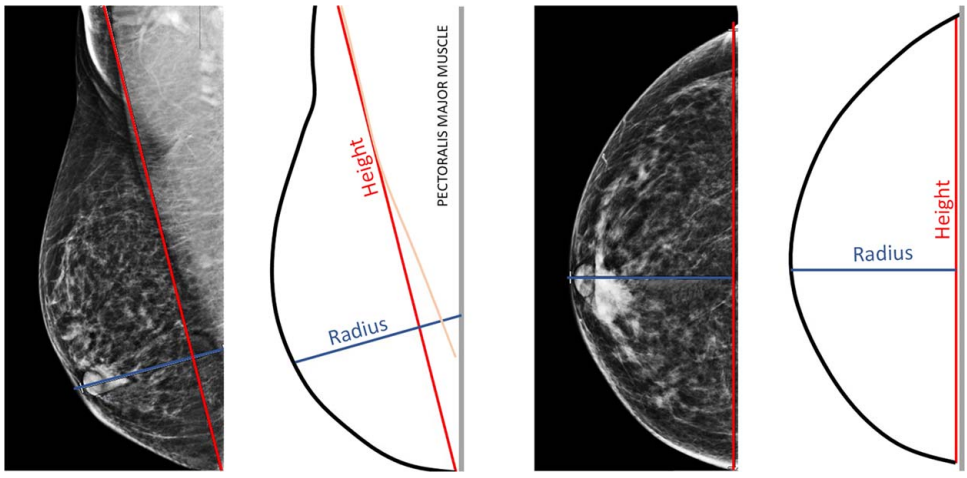

Figure 1. The Figure illustrates the measurement geometries for height and radius in the context of their application to calculate breast volume using the formula $1/3 \times \pi \times \text{Radius}^2$ (cc view) $\times$ Height (cc view).

Table 1

Summary of features for 200 breast cancers and comparison of features between negative and positive lymph nodes

Features	All ($N=200$) Mean ± SD	Lymph node positive ($N=84$) Mean ± SD	Lymph node negative ($N=116$) Mean ± SD	*P*
Age (year)				0.8764
< 49		27 (32%)	36 (31%)	
50–69		52 (62%)	73 (63%)	
> 70		5 (6%)	7 (6%)	
Tumour volume (mm^3)	10.65 ± 15.95	12.60 ± 18.26	9.24 ± 13.84	0.011
Breast volume (mm^3)	691.23 ± 615.88	641.18 ± 271.72	727.48 ± 774.55	0.696
Mass to breast ratio	0.0228 ± 0.0466	0.0247 ± 0.0472	0.0214 ± 0.0464	0.0431
	N (%)	*N* (%)	*N* (%)	*P*
Clinical T staging				
T1	68 (34.0)	23 (27.4)	45 (38.8)	0.236
T2	119 (59.5)	55 (65.5)	64 (55.2)	
T3	13 (6.5)	6 (7.1)	7 (6.0)	
Tumour location				
UOQ	97 (48.5)	48 (57.1)	49 (42.2)	0.13
UIQ	52 (26.0)	21 (25.0)	31 (26.7)	
LOQ	28 (14.0)	7 (8.3)	21 (18.1)	
LIQ	19 (9.5)	7 (8.3)	12 (10.3)	
Central	4 (2.0)	1 (1.2)	3 (2.6)	
Tumour histologic grade				
1		9 (4.5)	1 (1.2)	0.19
2		103 (51.5)	46 (54.8)	
3		64 (32.0)	30 (35.7)	
NA		24 (12.0)	7 (8.3)	
Lymphovascular invasion				
No		66 (33.0)	15 (17.9)	< 0.001
Yes		126 (63.0)	68 (81.0)	
NA		8 (4.0)	1 (1.2)	
Oestrogen receptor				
Negative	62 (31.0)	23 (27.4)	39 (33.6)	0.358
positive	138 (69.0)	61 (72.6)	77 (66.4)	
Progesterone receptor				
Negative	105 (52.5)	39 (46.4)	66 (56.9)	0.154
Positive	95 (47.5)	45 (53.6)	50 (43.1)	
HER-2				
Negative	93 (46.5)	32 (38.1)	61 (52.6)	0.046
Positive	107 (53.5)	52 (61.9)	55 (47.4)	
Tripple negative				
No	180 (90.0)	79 (94.0)	101 (87.1)	0.151
yes	20 (10.0)	5 (6.0)	15 (12.9)	

NA, not applicable.

LIQ, lower inner quadrant; LOQ, lower outer quadrant; UIQ, upper inner quadrant; UOQ, upper outer quadrant.

and type of surgery (mastectomy or breast-conserving surgery) did not demonstrate a significant independent association with lymph node metastasis in this analysis.

Discussion

The results of the study suggest that a higher tumour volume to breast volume ratio may be a significant predictive factor for axillary lymph node metastasis in breast cancer patients. This indicates that the relative proportion of tumour volume to the overall breast volume could play a role in determining the likelihood of lymph node involvement.

However, it is important to note that the statistical significance of the association diminishes in the multivariate analysis, suggesting that other factors may also contribute to axillary lymph node metastasis. Therefore, further research with a larger sample size is needed to confirm these findings and explore the potential influence of other variables.

In addition, calculating the tumour to breast volume ratio preoperatively can be challenging as precise tumour volume measurements are typically obtained from pathological examination of the surgical specimen. While imaging techniques such as MRI can provide estimates of tumour size, they may not provide exact tumour volumes. Future studies may benefit from incorporating more accurate preoperative imaging methods to assess tumour size and its relationship to breast volume.

Overall, the study provides valuable insights into the potential predictive value of the tumour to breast volume ratio in assessing axillary lymph node metastasis. However, further research and validation studies are necessary to fully understand its clinical implications and determine its usefulness in treatment decisions for breast cancer patients.

Conclusion

In conclusion, the study findings suggest that a higher tumour volume to breast volume ratio may serve as a significant predictive factor for axillary lymph node metastasis in breast cancer patients. This implies that the proportion of tumour volume relative to the overall breast volume could play a role in determining the likelihood of lymph node involvement.

The results highlight the importance of considering not only tumour size or T staging but also the tumour to breast volume ratio when assessing the risk of axillary lymph node metastasis. A higher ratio may indicate a greater tumour burden relative to the size of the breast, potentially indicating a more aggressive disease that is more likely to spread to the lymph nodes.

Ethical approval

Ethical approval for this study (Ethics Committee in Human Research Chiangrai Prachanukroh Hospital) was provided by protocol number EC CRH 067/65 In . Ethics Committee in Human Research Chiangrai Prachanukroh Hospital in ICH-GCP and ethical concern, Issued date: 24 January 2023.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Source of funding

No grants or financial support were received by any of the authors in relation to this study or to the writing of this article.

Author contribution

T.C.: writing manuscript , correspondent , interpretation of data and analysis. W.P.: interpretation of data. P.R.: acquisition of data. N.K.: collection of data. P.A.: collection of data. V.K.J.: collection of data. S.L.: collection of data. R.N.: collection of data.

Conflicts of interest disclosure

There is no conflict of interest.

Research registration unique identifying number (UIN)

The protocol had been registered at Thai Clinical Trials Registry (TCTR). The identification number is TCTR20230725005 (https://www.thaiclinicaltrials.org/show/TCTR20230725005).

Guarantor

Dr Tanet Chatmongkonwat.

Data availability statement

Publicly available.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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