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Value of sonomammography utilizing color Doppler technique in qualification of breast cancer patients for sentinel node identification

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Summary

Background: Sentinel node identification has become a standard procedure in the management of breast cancer. This procedure requires involvement of a multidisciplinary team and is rather costly. Ultrasonography (USG) of axillary lymph nodes is a method that gives hope for improving the quality of qualification of patients for the procedure.

Material/Methods: Eighty patients with grade I and II breast cancers underwent sentinel node identification followed by axillary lymphadenectomy. Pre-operative ultrasonography was employed to assess axillary lymph nodes, using the morphological and vascular characteristics as predictors of the presence of lymph node metastases.

Results: Sensitivity of sentinel node identification reached 89.3%, specificity – 100%, positive predictive value – 100%, negative predictive value – 93.5%, percentage of false negative results – 10.7%. Sensitivity of USG reached 68.75 %, and specificity – 70.31%. In the group of patients in whom the sentinel node was identified, the sensitivity of the method was 69.23 %, and specificity – 72.41%.

Conclusions: Preoperative axillary lymph node ultrasonography in breast cancer patients, utilizing color Doppler technique, allows better selection of patients for sentinel node identification procedure.

Key words: breast cancer • lymph node ultrasonography • sentinel node identification

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Background

The presence, or absence, of metastases in axillary lymph nodes of breast cancer patients has been, to date, the most important known prognostic factor [1]. The ability to metastize, to release tumor cells which invade the surrounding stroma, lymphatic and blood vessels, is determined first of all by the biology of the primary tumor [2]. However, the attempts to assess the axillary nodal status on the basis of findings from tumor histopathology are associated with too high false negative rates to apply into clinical practice [3, 4]. Also clinical examination does not allow reliable assessment of nodal status, because the results of this examination are consistent with the ultimate histopathological results obtained for the specimens only in ca. 50% of cases [5]. Therefore, axillary lymphadenectomy was, up to the recent times, the only method which allowed to obtain information concerning the presence of metastatic lymphadenopathy. However, the procedure has a significant impact of the patients' quality of life, affected by complications such as lymphatic cysts, impaired shoulder girdle mobility range at the side of the surgery, and innervation disturbances in the area supplied by the intercostobrachial nerve [6, 7]. Less common complications, which can, however, become persistent, include lymphedema of the arm [8].

In the countries which introduced mammography screening for breast cancer, ca. 70% of women diagnosed with the disease has no metastases in the axillary lymph nodes. For this reason, the recently introduced method of sentinel lymph node (SLN) identification has become acceptable for making it possible to avoid resection of axillary lymph nodes if they contain no metastases [9]. The procedure, despite much lower invasiveness for the patient, is associated with high costs incurred by the necessity to purchase expensive radio-labeled agents and to engage a multidisciplinary team indispensable to perform it correctly. Additionally, ca. 30% of patients still requires axillary lymphadenectomy because of tumor cell metastases in the sentinel lymph node.

Therefore, more precise preoperative assessment of axillary lymph nodes would allow more appropriate qualification, excluding the patients in whom the probability of metastases in the axillary lymph nodes is low.

Employing ultrasonography (USG) for examination of axillary lymph nodes may lead to significant improvement of their clinical assessment, and, consequently, improve the quality of qualification of breast cancer patients for sentinel node identification procedures.

Materials and methods

Ultrasonographic lymph node assessment was performed in 80 patients aged 33–79 (mean age – 53.9 years) with

Table 1. Clinical characteristics of the studied group of patients and histopathological features of the primary tumors.

Characteristics	Number of patients	%
Tumor size (mm):		
≤ 20	44	55
> 20	24	30
Microcalcification	6	7.5
Determination impossible[a]	6	7.5
Side of the body:		
Right breast	41	51.25
Left breast	39	48.75
Histological type:		
Ductal	59	73.75
Lobular	9	11.25
Others	12	15.0
Grade of histological differentiation[b]:		
G1	11	18.33
G2	28	46.67
G3	21	35.0
LVSI[c]:		
Present	14	17.5
Absent	66	82.5
Metastases to axillary lymph nodes:		
Present	30	37.5
Absent	50	62.5
Invasive preoperative diagnostics method:		
Open excisional biopsy	21	26.25
Percutaneous large core needle biopsy	59	73.75
Surgery type:		
Conservative surgery	27	33.75
Modified radical mastectomy	53	66.25

[a] tumor fragmentation after open surgery excisional biopsy made it impossible to assess precisely the tumor size on histopathology;
[b] In 20 cases histological differentiation was impossible to assess; [c] LVSI – lymphatic vessels and spaces infiltrated by tumor cells.

Table 2. Results of sentinel node identification in the analyzed group.

Sentinel node	Other axillary lymph nodes	Number of patients (%)
(+)[a]	(+)	25 (35.2)
(-)[b]	(-)	43 (60.6)
(-)[b]	(+)	3 (4.2)
Total		71 (100)

IDENTIFICATION INDEX (71/80 patients) = 88.75%; [a] (+): metastases present; [b] (-): metastases absent

primary breast tumors, scheduled for, and subjected to, sentinel node identification. Then all the patients underwent elective axillary lymphadencetomy.

Pre-invasive lesions, multiple tumor foci localized in different quadrants of the brease (multifocal hyperplasia), the primary tumor size exceeding 5 cm, suspicion of metastases to the regional lymph nodes based on clinical examination, as well as planned neo-adjuvant therapy provided contraindications for participation in the study. Pregnancy, lactation, coincident tumors in other localizations, or condition after anti-tumor therapy also constituted the exclusion criteria. Clinical characteristics of the analyzed group of patients and histopathological characteristics of primary tumors are presented in table I.

Criteria of axillary lymph nodes assessment with ultrasound

Ultrasonography was performed by 3 authors of the paper (PB, KWJ, WK) before the surgery, using a multiple-channel (1024 channels) US madine, equipped with a variable frequency (7.5–12 MHz) probe, color Doppler imaging module and 3D/4D imaging module (Voluson 730 Pro; Kretztechnik, GE). The lymph node assessment took into consideration, first of all, the shape, appearance of the medullary portion of the lymph node (hilus), vascular pattern, structure of the cortical portion and size. With respect to shape, the horizontal to vertical axis ratio („L/T ratio") was noted. If it was ≥ 2, the node was considered to be in normal condition; if the ratio was < 2, it was considered to be suspicious of the presence of metastases. In case of irregular contours of the hilus, or its compression by abnormally enlarged cortical portion, such a pattern was also regarded as suspicious. The presence of blood vessels entering the lymph node in the regions other than the hilus was also qualified as suspicious, as well as node diameter exceeding 2.5 cm.

Statistical analysis

The obtained results were subjected to statistical analysis employing the elements of descriptive statistics. Sensitivity, specificity, positive and negative predictive values (PPV and NPV), percentage of false negative results (FNR) were calculated for the procedure of sentinel node identification. The correlation between ultrasound examination results and the axillary lymph nodes status as assessed by histopathology was calculated using Ch^2 test, with $p < 0.05$ adopted as the significance level.

Results

The sentinel node(s) was (were) identified and resected in 71 patients. In the whole study group of 80 patients, the presence of metastases in lymph nodes was detected in 30 cases. Tumor cell metastases were found in 25 of the patients with identified sentinel nodes. In 68 cases, the histological condition of the lymph node(s) correctly reflected the histological condition of the remaining resected axillary lymph nodes. In 3 cases, the sentinel node did not contain tumor cells, whereas they were revealed by histopathology in the remaining resected axillary lymph nodes. The results of sentinel node identification in the studied group are presented in table II. The sensitivity of the

Table 3. Comparison of USG assessment with histopathology results.

Suspicion of the presence of metastases on USG	*Presence of metastases confirmed on histopathology*		*Total*
	(+)	(-)	
(+)	11	5	16
(-)	19	45	64
Total	30	50	80

p< 0.01

Table 4. Comparison of USG assessment with histopathology results in the group with correctly identified sentinel node(s).

Suspicion of the presence of metastases on USG	*Presence of metastases confirmed on histopathology*		*Total*
	(+)	(-)	
(+)	9	4	13
(-)	16	42	58
Total	25	46	71

p< 0.01

Figure 1. Abnormal hilus shape of invaded lymph node.

method, calculated on the basis of the obtained results, was 89.3%, specificity – 100%, positive predictive value – 100%, negative predictive value – 93.5%, percentage of false negative results – 10.7%.

In the study group of 80 patients, the presence of metastases in axillary lymph nodes was suspected on the basis of USG in 16 cases. In 11, this preliminary diagnosis was confirmed by the ultimate results of histopathology of lymph node specimens. The sensitivity of USG was 68.75%, specificity – 70.31% (table III). In the group of patients who underwent sentinel node identification, lymph node metastases were suspected in preoperative USG in 13 cases. The suspicion was confirmed in 10 patients, including 9 from the group with correctly identified sentinel nodes. The sensitivity of the method in the latter group was 69.23%, and specificity – 72.41% (table IV). The correlation between assessment of axillary lymph nodes by USG and their actual condition determined by histopathology was significant statistically ($p < 0.01$).

Analyzing the characteristic features of US images which indicated the possibility of tumor cell metastases to axillary lymph nodes, it was concluded that the most frequently observed abnormality was the hilus shape (figure 1), and reduced value of horizontal to vertical lymph node axis ratio (L/T ratio < 2) (figure 2). The presence of abnormal blood vessels penetrating the capsule in color Doppler results was associated in each case with the presence of lymph node metastases (figure 3).

Discussion

Ultrasonography is a method which allows the physician experienced in US diagnostics of the mammary gland to visualize the axillary lymph nodes. The sensitivity of assessment of lymph node metastases with this method

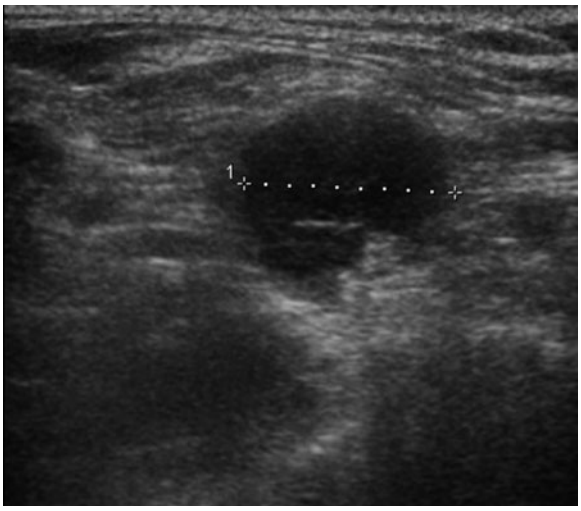

Figure 2. Round-shape lymph node.

ranges from 36 to 87%, and specificity from 56 to 95% [10]. Thus, the efficiency range of this method is much better than that of clinical axillary lymph node assessment by palpation, but not as much as to abandon histopathological verification.

On US assessment of lymph nodes, the attention is often directed primarily to their size. However, unlike other diagnostic methods such as mammography, computed tomography or magnetic resonance, ultrasonography allows to assess not only the size, abut also the morphology of lymph nodes. The lymph node must contain a considerable number of tumor cells to become significantly enlarged (the size > 2.5 cm has been adopted as a criterion in this study). In the lymph nodes, tumor cell colonization process starts from the subcortical layer, and then involves the cortex, causing compression of the medullary portion. In such a situation, US images first reveal a distortion and then complete abolition of the hyperechogenic hilus pattern [11, 12].

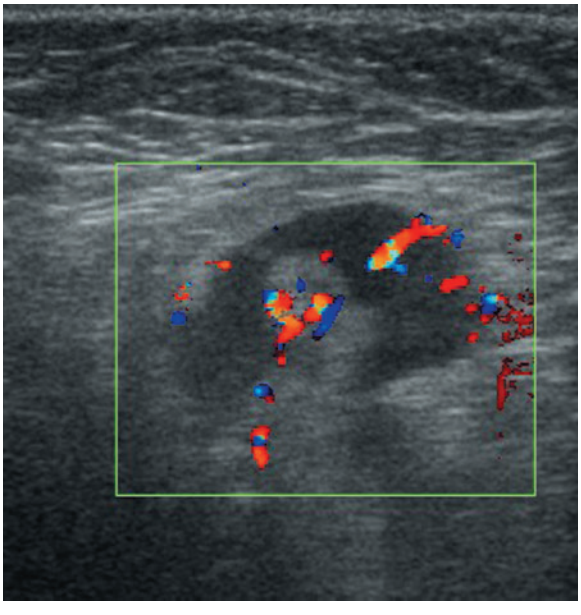

Figure 3. Transcapsular new blood vessels of the lymph node.

Such an image, referred to by Sakai et al. [13] as „roundness index" (L/T ratio) was the most frequent symptoms serving as the basis for lymph node qualification as suspicious of metastases. That symptom was also more often correlated with positive histopathology results than isolated increase of lymph node diameter. Interesting observations were contributed by introduction of color Doppler in the examination of axillary lymph nodes. Although observation of lymph node enlargement, even beyond 3 cm in diameter, was often of reactive character, the presence of blood vessels penetrating the capsule was in all cases associated with the presence of tumor metastases. The above results confirm the reports concerning the pathognomonic significance of that symptom [14].

SLN identification provides an attractive alternative for total axillary lymphadenectomy in patients with no axillary lymph node metastases. However, in the patients with axillary lymph node involvement, the procedure is not necessary. Applied it for that patients, the procedure may sometimes even sometimes lead to inappropriate staging of the disease, e.g. in the case of false negative results of sentinel node identification. Such results may happen when bulky metastases present in the sentinel node block tracer or dye uptake and cause collateral lymph flow to other lymph nodes [15].

In assessment of the value of ultrasonography applied before the procedure of SLN, the specificity of the examination, i.e. as high as possible consistency of the US diagnosis with the actual node status, is especially important. In the analyzed group of 80 patients, 16 were suspected of lymph node metastases, which were confirmed in 11. The specificity of USG in that group was 70%, and in the group with correctly identified sentinel node(s), slightly higher – 72%. It can be presumed that supplementing US diagnostics with aspiration biopsy of the suspicious lymph node(s) could improve these results significantly. Because of the presence of large blood vessels in the region, application of core needle biopsy arouses some doubt in this case. However, such method also has its supporters [16]. Therefore, summing up the observations resulting from this study, it can be concluded that assessment of axillary lymph nodes with USG is a valuable method complementary to the diagnostics preceding sentinel node identification procedures in patients with breast cancer. It should be considered whether the cases with completely abolished hilus hyperechogenicity, or the presence of blood vessels penetrating the capsule, should provide an indication for cytological or histological verification by biopsy. Obtaining the answer to this question would allow to limit the use of sentinel node identification procedures in the cases in which the patients do not benefit from its application.

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