Influence of the imaging method and histopathological features on preoperative size prediction of ductal carcinoma *in situ* (DCIS) of the breast

Wpływ badań obrazowych i czynników histopatologicznych na przedoperacyjne prognozowanie wielkości DCIS piersi

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Summary

Aim of the study: The aim of the study was to evaluate the accuracy of mammography and ultrasonography in predicting preoperative DCIS size compared to final histopathologic measurement of the extent of DCIS.

Material and methods: A retrospective analysis was performed of the clinical, histopathological and imaging records of 32 consecutive female patients initially treated by breast-conserving surgery for DCIS between 1999 and 2005. Group 1 consisted of 19 female patients with a palpable breast tumor, while group 2 comprised 13 female individuals with no palpable breast lesion. All patients were preoperatively diagnosed with biopsy.

Results: In group 1, mammography size was smaller than histopathological size in 14 patients (73.68%), while they were equal in 5 cases (26.31%). However, in group 2, mammography size was the same as histopathological size in 5 cases (38.46%), but was smaller in 8 individuals (61.53%).

The degree of the underestimations for both imaging methods compared to pathological size were identical, with a value of 1.1 ±0.9 cm and 1.2 ±1.1 cm for groups 1 and 2, respectively.

Furthermore, in both study groups, as final histopathologic size decreased, the degree of underestimation increased ($p < 0.05$).

Conclusions: The present study demonstrates that smaller DCIS pathological size is associated with greater discrepancies in imaging method size prediction.

Key words: DCIS, size prediction of tumor, mammography, ultrasonography.

Streszczenie

Cel pracy: Celem badania była ocena dokładności mammografii i ultrasonografii w przedoperacyjnym prognozowaniu wielkości DCIS w porównaniu z ostateczną wielkością DCIS określoną w badaniu histopatologicznym.

Materiał i metody: Retrospektywna analiza została przeprowadzona na danych klinicznych, histopatologicznych oraz wynikach badań obrazowych 32 chorych kobiet leczonych z powodu DCIS za pomocą terapii oszczędzającej pierś w latach 1999–2005. Grupa 1. składała się z 19 kobiet z wyczuwalnym palpacyjnie guzem piersi, a grupa 2. składała się z 13 kobiet z niewyczuwalnym palpacyjnie guzem. U wszystkich chorych wykonano przedoperacyjnie biopsję.

Wyniki: W grupie 1. u 14 (73,68%) chorych wielkość DCIS w mammografi była mniejsza niż w ostatecznym badaniu histopatologicznym, a w 5 (26,31%) przypadkach taka sama. Natomiast w grupie 2. ocena wielkości DCIS była jednakowa w mammografii i badaniu histopatologicznym u 5 chorych (38,46%), a mniejsza w mammografii w 8 (61,53%) przypadkach. Stopień niedoszacowania wielkości guza był taki sam dla obu metod obrazowych i wynosił odpowiednio 1,1 ±0,9 cm i 1,2 ±1,1 cm dla grupy 1. i 2. Ponadto w obu badanych grupach im mniejsza była ostateczna wielkość guza w badaniu histopatologicznym, tym większy był stopień niedoszacowania wielkości guza w badaniach obrazowych ($p < 0.05$).

Wnioski: W badaniu wykazano, iż im mniejsza jest wielkość DCIS określona w ostatecznym badaniu histopatologicznym, tym większa jest niedokładność w przedoperacyjnym prognozowaniu wielkości guza w badaniach obrazowych.

Słowa kluczowe: DCIS, prognozowanie wielkości guza, mammografia, ultrasonografia.

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Introduction

Ductal carcinoma *in situ* (DCIS) of the breast is a noninvasive malignant tumor located in the mammary ducts. In a DCIS neoplasm, the proliferation of malignant cells is limited only to the epithelium without invasion into the periductal stromal tissue [1, 2]. In recent studies, DCIS was diagnosed in 15% to 30% of all breast carcinomas. In between 25% and 56% of clinically occult breast cancers, DCIS was detected mammographically [1, 2]. DCIS is regarded as a potential precursor of invasive carcinoma and a risk factor for the development of cancer in the same or contralateral breast [3, 4].

Mammography is a very useful method for the detection of DCIS, however, it has poor accuracy in cases which lack microcalcifications [5, 6]. In mammography, 62-98% of DCIS are recognised by microcalcifications, whereas only 2-23% of DCIS are associated with other symptoms: focal mass, asymmetric density or architectural disorder [7]. However, a large number of DCIS (6-23%) tumors are not detectable by mammography [8, 9].

The role of ultrasonography in DCIS detection is still under discussion. Some authors have proposed a limited application of ultrasound imaging in the diagnosis of DCIS, as it can be a particularly useful tool in the evaluation of non-calcified DCIS, not only in detecting the lesion but also in evaluating its size [10]. Furthermore, ultrasound imaging enables the detection of mammographically occult DCIS in patients with dense breasts [11].

Percutaneous biopsy is the most effective technique for preoperative breast tumor diagnosis. While core needle biopsy is recommended as a more accurate 'gold standard' in this regard, ultrasound-guided fine needle aspiration biopsy is still in use due to its availability and for economic reasons [13, 14].

Breast-conserving surgery has become the standard method of treatment for DCIS. However, some patients require more than one surgical procedure to achieve clear histological margins because of inadequate excision [1]. Therefore, an exact description of DCIS size is essential to avoid recurrence.

The aim of the present study was to perform a retrospective evaluation of the accuracy of mammography and ultrasonography in predicting preoperative DCIS size compared to final histopathologic measurement of the extent of DCIS. The impact of other related clinical and histopathological factors was also investigated.

Material and methods

Patients

The patients' age ranged from 48 to 68 years (average age 57.39 ±10.61 years). All patients were in the menopausal period.

The patients whose postoperative histopathological diagnosis revealed neoplasms other than DCIS cancer were excluded from the analysis. Other exclusion criteria were previous history of any other malignancy, previous breast surgery, family history of breast malignancy and premenopausal age.

The analyzed patients were divided into two groups. Group 1 consisted of 19 female patients with a palpable breast tumor, while group 2 comprised 13 female individuals with no palpable breast lesion: the breast tumors in group 2 being detected during mammography screening. All patients were preoperatively diagnosed with either core needle biopsy or ultrasound-guided fine needle biopsy.

Imaging data

The following mammographic and ultrasound features were analyzed: size, presence of calcifications, mammographic density, parenchymal pattern and BIRADS classification.

Histopathological assessment

The histopathological results were analyzed with particular attention being paid to the size, grade and surgical margin. A histological margin of 10 mm was required. Cases in which this was not achieved during the first operation proceeded to reexcision or mastectomy.

Statistical analysis

The relationships between age, mammographic and histopathological size, density and grade were evaluated using the χ^2 test. All other variables were analysed using ANOVA.

Results

Both study groups were comparable according to demographic characteristics. The mean age of the patients did not differ significantly between the groups. It was found to be 61 ±10.2 and 63 ±9.5 for group 1 and 2, respectively.

The imaging features are presented in Tables I and II, and the pathological features in Tables III and IV. In no patient was the mammographical or ultrasound extent larger than histopathological extent. In group 1, mammography size was smaller than histopathological size in 14 patients (73.68%), while they were equal in 5 cases (26.31%). However, in group 2, mammography size was the same as histopathological size in 5 cases (38.46%), but was smaller in 8 individuals (61.53%).

In group 1, ultrasound measurement indicated that tumor size was smaller than the histopathological di-

Table I. Mammographical features of DCIS patients

Patients	Size (mean)	Presence of calcifications (no. of patients)	Density (no. of patients)		BIRADS (no. of patients)						
			high	low	0	1	2	3	4	5	6
Group 1	2.2 ±1.2 cm	15	3	1	–	–	4	3	12	–	–
Group 2	1.3 ±1.5 cm	13	–	–	–	–	–	3	10	–	–

Table II. Ultrasound features of DCIS patients

Patients	Size (mean)	Presence of calcifications (no. of patients)	Echogenic (no. of patients)		BIRADS (no. of patients)						
			hyper	hypo	0	1	2	3	4	5	6
Group 1	2.1 ±1.5 cm	14	–	5	–	–	4	3	12	–	–
Group 2	1.4 ±1.9 cm	13	–	13	–	–	–	2	11	–	–

Table III. Histopathological factors of DCIS patients

Patients	Size (mean)	Grade (no. of patients)		Margin (no. of patients)	
		high	low	< 10 mm	> 10 mm
Group 1	2.5 ±1.8 cm	12	7	6	13
Group 2	1.6 ±1.7 cm	7	5	5	8

Table IV. Results of preoperative biopsy of DCIS patients

Patients	Fine needle aspiration biopsy (no. of patients)			Core needle biopsy (no. of patients)		
	cancer cells	suspicion	benign or non-diagnostic	cancer	suspicion	benign or non-diagnostic
Group 1	8	4	0	5	0	2
Group 2	1	6	4	2	0	0

ameter in 10 patients (52.63%), but identical in 9 cases (47.36%). However, in group 2, the ultrasound diameter was smaller than the histopathological size in 8 cases (61.53%), and was identical in 5 patients (38.46%). The above mentioned percentage schedule of imaging methods size prediction between groups 1 and 2 is statistically insignificant.

The underestimation appeared in patients with the tumor size < 1.5 cm and < 1 cm in groups 1 and 2, respectively: this correlation is statistically significant ($p < 0.05$).

The degree of the underestimations for both imaging methods compared to pathological size were identical, with a value of 1.1 ±0.9 cm and 1.2 ±1.1 cm for groups 1 and 2, respectively.

Furthermore, in both study groups, as final histopathologic size decreased, the degree of underestimation increased ($p < 0.05$).

Necrosis, calcification, density, BIRADS scale, histological grade, surgical margins or biopsy result were not found to have any association with the differences in tumor size evaluated by the imaging method (mammography, ultrasound) and pathologic measurement.

Insufficient surgical margins were noted only in cases where the true histopathological diameter of the tumor was underestimated by mammography and ultrasonography.

Discussion

Little data exist regarding the accuracy of imaging methods in predicting DCIS size. Chakrabarti *et al.* report mammography to be 73% accurate in predicting histological extent within 10 mm [15]. However, in contrast to the present study, the authors found the pathological size to be underestimated by > 10 mm in 17.2% of their patients and overestimated by > 10 mm in 10.2%. The overestimation was explained by collecting the tumor sample during core needle biopsy and the presence of benign calcifications.

The mammographic size is currently the standard method for estimating pathological size preoperatively, but underestimation is believed to occur in approximately 15-20% of cases [16, 17]. However, our study showed the tumor to be underestimated in 73.68%. This difference may result from the limited number of patients in our study and the use of retrospective analysis.

Microcalcification is a very characteristic radiological feature of DCIS, present in 85-90% of cases. Calcifications occur in high grade invasive carcinoma as well as in benign lesions [16]. Due to the potential inaccuracies caused by calcification, and the fact that some cases of DCIS are mammographically occult, ultrasonography may be considered for the detection of

DCIS not associated with microcalcifications [17]. Typical DCIS ultrasound features are mass without microcalcifications, mass with microcalcifications, isolated microcalcifications, ductal changes and dimensions over 20 mm [18]. DCIS ultrasonography is the most accurate in the event of the co-occurrence of the above mentioned features [18].

In our study, all patients in whom DCIS extent was underestimated required a further surgical procedure. The most important factor ensuring a complete excision is the size of the excision margin taken. Some studies have shown that the percentage of patients with a complete excision is 66% when a 10-mm excision margin is taken, compared to 83% and 89% for a 20-30 mm excision margin [15, 19].

Other studies have demonstrated that the use of a large margin can reduce the effect of underestimating the pathological size by mammography or ultrasonography. Several studies have also confirmed that larger margin widths are associated with a reduced risk of local recurrence [20-22].

Although most authors report that larger mammography size is associated with underestimation [15, 21], the present study does not confirm this. In our series, the disparity between the results of the imaging and pathological tests was correlated with final pathological diameter.

Holland *et al*. demonstrate a greater disparity between mammographic and pathological size for cribriform and micropapillary histological type DCIS (47% underestimation > 20 mm) vs. comedo DCIS (16% overestimation by > 20 mm) [19].

Magnetic resonance mammography seems to be a method with higher accuracy in DCIS detection compared to mammography and ultrasonography. The prospective study on women with an increased risk of breast cancer showed that magnetic resonance mammography detects DCIS in 15% of patients without any lesions in mammography and ultrasonography [23].

However, final pathological size depends on the histopathological method used in the laboratory. Faverly *et al.* showed that the choice of the procedure used in taking sections has an influence on the diagnosis of multifocal or continuous intraductal growth, as does the differentiation of DCIS: well-differentiated lesions are usually multifocal [16]. Moreover, the histopathological diagnosis is impeded by coexisting DCIS with other breast neoplasms, especially Paget disease. Marczyk *et al.* described similar proliferative activity of malignant cells, measured as Ki-67 antigen expression, in Paget disease and DCIS. Additionally, DCIS presented overexpression of c-erbB2 as well as Paget disease [24].

Except for medical reasons, the high accuracy and quality of the imaging method in breast cancer diagnosis is important due to encouraging women to participate in the breast cancer screening programme [25].

Conclusions

The present study demonstrates that smaller DCIS pathological size is associated with greater discrepancies in imaging method size prediction. No other preoperative clinical and pathological factors were identified.

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