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A 7-year experience in core needle biopsy of breast lesions: Correlation between imaging and hematoxylin and eosin-stained sections

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Abstract: Screening mammography is an imaging procedure which allows breast cancer detection in its early stage. The Breast Imaging and Reporting Data System (BI-RADS) determined six radiological categories for describing lesions. The core needle biopsy (CNB) is minimally invasive procedure that provides pathohistological samples. *Via* microscopic analysis, samples are categorized into five groups according to the B system for pathohistological report. The aim of the study was to follow the spectrum of pathohistological diagnoses; to define which BI-RADS and core categories are most commonly expressed in certain age groups; and to determine the incidence of histological diagnoses in different BI-RADS categories. The study included 631 patients and data was analysed in order to localise the lesion, BI-RADS and core category and pathohistological diagnosis. Within 631 biopsies, 33 diagnoses were given. In each age group, the findings indicating a high risk for malignancy were the most common (>2 %). The highest percentage of malignant categories was found in patients over the age of 61. Final diagnoses showed a deviation compared to the radiological categories, especially in BI-RADS4 category. Pathohistological diagnosis is always a definite confirmation of a breast lesion type and it has significant contribution to the evaluation of CNB quality.

Keywords: mammography; BI-RADS; histology; breast.

INTRODUCTION

Breast cancer is the second most common cause of death due to malignancy in women worldwide. Mortality rate is estimated to be 6.6 %, with the global incidence being 11.6 %. In East Europe, the incidence is 54.5 % and mortality rate peaks 15.5 % in women aged 40–60 years.[1,2] National guidelines for malig-

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nancy prevention in primary health services give following propositions: guide for self-examination in women who are up to 30 years old, once-a-year clinical examination for women older than 40 and the screening mammography for women aged 45–69 years once in two years.[3–5] Screening mammography is an imaging technique based on use of low energy X-rays, which provides the detection of breast cancer in its earliest stage of growth, before the disease is clinically manifested. This procedure gives the opportunity to detect lesions smaller than 2 cm in diameter, for both *in situ* and invasive carcinoma.[4–6] The advantage of this method is its ability to detect microcalcifications which are often the only sign of *in situ* carcinoma. On the other hand, the sensitivity of mammography is 85 % and only 65 % in women with high breast density. Specificity of the method is about 90 %, however, the reproducibility is limited because of radiation that needs to be reduced to lower values.[7] The Breast Imaging Reporting and Data System (BI-RADS), established by the American College of Radiology (ACR), defined the categories of mammography results, marked as BI-RADS 0–6. BI-RADS4 category was further subcategorized into A, B and C (with 2––10 %; 11–50 and 51–95 % malignance probability, respectively).[8] In the case of palpable lesions suspicious of malignancy during the clinical examination (categories K3, K4 and K5) or the mammography results suspicious of malignancy, patients are suggested to undergo following methods: fine needle aspiration biopsy (FNAB), vacuum assisted biopsy (VAB) or core needle biopsy (CNB). These procedures are performed for the purpose of definite pathohistological diagnosis. The percutaneous biopsy methods of non-palpable lesions could be conducted with the navigation of imaging methods such as ultrasonography, stereotaxic mammography or MRI.[9] The core needle biopsy is minimally invasive procedure which allows the tissue sampling through the incision of small diameter made by radiologist. The sensitivity of CNB is 97–99 %. The CNB categories are defined as B1–B5, where B5 category is further subcategorized into: B5a (*in situ*), B5b (invasive carcinoma), B5c (invasion cannot be determined) and B5d (malignant phyllodes tumours, lymphoma, sarcoma and metastases).[10]

The aim of this study was to define the spectre of pathohistological diagnoses in the Centre for Pathology and Histology in the University Clinical Centre of Vojvodina after a radiological diagnostic procedure in a 7-year period, to emphasize the most common BI-RADS and CNB categories in certain age groups, and to make a preview of specific diagnoses which were preliminary defined by the BI-RADS system.

EXPERIMENTAL

In a 7-year period, the cases of 631 patient were reviewed in this retrospective study. The study was conducted in the University Clinical Centre of Vojvodina and approved by the Research Ethics Committee of this institution. The study obtained radiology reports categorized as BI-RADS 0–5, and based on age, anamnestic data and clinical examination, the pre-

cise indications for CNB were stated. The exclusion criteria used in this study referred to patients with VAB samples, metastatic lesions and lesions without neoplastic predisposition. Tissue samples were fixed by 10 % neutral formalin, then routinely paraffin-embedded and cut at approximately 5-mm intervals, sliced to 4-μm-thick sections and stained with hematoxylin and eosin (H&E). The lesions were categorized according to the European Society of Breast Cancer Specialists and Biopsy reporting the category system as B0 (inadequate sample), B1 (normal breast tissue), B2 (benign), B3 (uncertain malignant potential), B4 (suspicious of malignancy) or B5 (malignant). Histologic grade (1, 2 or 3), nuclear pleomorphism (1, 2 or 3) and mitoses per 10 high power fields (HPF) were counted and defined in cases of malignant neoplasm. The grade of malignant lesions was determined according to the Nottingham prognostic index as: Grade I = summary result 3, 4 or 5, Grade II = summary result 6 or 7 and Grade III = summary result 8 or 9.[8] The data was processed in the Microsoft Excel 2016 and the results were presented in tables through percentages.

RESULTS AND DISCUSSION

Based on age distribution, 631 patient was divided into 6 categories with different percentage presentation: <30 (1.11 %), 31–40 (5.86 %), 41–50 (12.20 %), 51–60 (31.22%), 61–70 (44.06%) and >70 years of age (5.55 %). The presentation of certain BI-RADS categories in different age groups was shown in Table I. The most common BI-RADS categories were 4a, 4b and 5. The predominant categories within age groups were: <30: BI-RADS4a; 31–40: BI-RADS3; 41–50: BI-RADS4a; 51–60: BI-RADS4b; 61–70: BI-RADS4b; >70: BI-RADS4b and 5.

TABLE I. BI-RADS categories in different age groups given as presentation in certain age groups in %

BI-RADS	Summary presentation, %	Group					
		<30	31–40	41–50	51–60	61–70	>70
0	0.95	0	0	0	0.48	0.32	0.16
1	0	0	0	0	0	0	0
2	4.28	0	0.32	0.63	0.9	1.27	0.16
3	8.87	0.16	2.22	1.58	2.38	2.22	0.32
4a	30.12	0.53	1.53	4.44	9.50	13.21	0.90
4b	30.59	0.21	0.9	3.01	10.14	14.47	1.85
4c	9.83	0.21	0.42	1.27	2.85	4.33	0.74
5	1.37	0	0.48	1.27	3.96	8.24	1.85

Table II shows the frequency of CNB categories and the presentation in different age groups. The predominant categories within age groups were: <30: B4; 31–40: B2; 41–50: B2; 51–60: B2; 61–70: B5; >70: B5.

Tables III and IV present all histological diagnoses after the core needle biopsy and their percentage within BI-RADS categories which indicated the biopsy at the first place.

The breast morphology changes from early adolescence to menopause under the influence of sex hormones. The breast structure significantly influences the inter-

TABLE II. Frequency of CNB categories and presentation in certain age groups given as representation of CNB categories in specific age groups in %

CNB	Representation of CNB categories in summary results, %	Group					
		<30	31–40	41–50	51–60	61–70	>70
B1	11.41	0.79	0.79	0.95	3.80	5.71	0.16
B2	47.86	3.02	3.80	7.13	17.12	18.07	1.74
B3	1.90	0.16	0.16	0	0.63	0.95	0.16
B4	0	0	0	0	0	0	0
B5	38.19	0.48	1.11	4.12	9.67	19.33	3.49

TABLE III. Diagnostic specter in the preliminary determined BI-RADS categories 0, 2 and 3

BI-RADS 0	BI-RADS 2	BI-RADS 3
B1: No morphological changes or cell atypia (0.48 %)	B1: No morphological changes or cell atypia (0.79 %)	B1: No morphological changes or cell atypia (1.43 %)
B5: DCIS (0.16 %)	B2: Adenosis (0.16 %)	B2: Adenosis (0.48 %)
	Apocrine metaplasia (0.48 %)	Sclerosis and microcalcifications (0.32 %)
	Fibrosis (0.32 %)	
	Fibrocystic change (0.48 %)	
	Fibroadenoma (1.11 %)	
	Gynecomastia (0.16 %)	
	Ductal hyperplasia (0.16 %)	
	Steatonecrosis (0.16 %)	
	B3: Uncertain malignant potential (0.16 %)	B5: DCIS (0.64 %)
		Invasive lobular carcinoma (0.16 %)
		Invasive carcinoma of no special type (0.16 %)
	B5: Invasive ductal carcinoma (0.16 %)	

pretation of mammographic results and fibroglandular breast composition aggravates further BI-RADS classification, thus also the indications for CNB. From the total number of newly ill, 30 % of patients is younger than 50, and approximately 33 % are from 50 to 64 years of age.[11–13] In our regional centre, mammography was most commonly performed in women from 51 to 70 years of age (75.27 %), and the most common categories were BI-RADS4 and BI-RADS5 (76.08 %). CNB is the method of choice in diagnosis of papillary lesions, but it is unreliable for differentiating fibroadenoma from phyllodes tumour (B3) in cases of fibroepithelial lesions.[13] The tissue volume obtained during CNB is smaller than the volume obtained during VAB.[14] The number of false negative CNB results compared to open excision biopsy (OEB) is 1.4 % for biopsies performed with 16G and 18G needles. The biggest concordance is proven in the cases of diagnosing lesions larger than 10 mm. The sensitivity of CNB method rises with the size of specimen, number of calcifications and it is dependent of tumour type.[15] It is better to opt for CNB in cases of palpable lesions or those with micro-

TABLE IV. Diagnostic specter in the preliminary determined BI-RADS categories 4 and 5

BI-RADS 4a BI-RADS 4b BI-RADS 4c	BI-RADS 5
B1: No morphological changes or cell atypia (8.72 %)	B1: No morphological changes or cell atypia (0.16 %)
B2: Adenosis (2.85 %)	B2: Adenosis (0.16 %)
Pseudoangiomatous stromal hyperplasia (0.16 %)	
Mastitis (1.43 %)	
Papillomatosis (0.32 %)	
Intraductal papilloma (1.27 %)	
Steatonecrosis (1.11 %)	
Sclerosis and microcalcifications (3.64 %)	
Postradiation stromal atypia (0.16 %)	
B3: Uncertain malignant potential (0.95 %)	B5: LCIS (0.16 %)
Phyllodes tumor (0.32 %)	Invasive ductal carcinoma (10.94 %)
	Invasive lobular carcinoma (1.11 %)
	Micropapillary carcinoma (0.16 %)
	Mucinous carcinoma (0.16 %)
	Mixed carcinoma (0.16 %)
	Cribriform carcinoma (0.16 %)
	Tubulolobular carcinoma (0.16 %)
	Invasive carcinoma of no special type (0.48 %)
B5: DCIS (0.95 %)	
Invasive ductal carcinoma (16.48 %)	
Invasive lobular carcinoma (3.01 %)	
Micropapillary carcinoma (0.32 %)	
Mixed carcinoma (0.32 %)	
Mucinous carcinoma (0.64 %)	
Metaplastic carcinoma (0.16 %)	
Invasive carcinoma of no special type (0.48 %)	
Neuroendocrine carcinoma (0.16 %)	

calcifications. If a clinical or radiological assessment indicates cystic lesion, a better approach is through the fine needle aspiration cytology (FNAC).[16] In a systematic meta-analysis from Wang *et al.*, the results pointed to a better sensitivity of CNB than FNAC in the evaluation of suspicious breast lesions.[17] Even though FNAC is a less invasive and easily reproducible modality, the differentiation of fibroadenoma and *in situ* carcinoma cannot be made by this method.[16] The indicative radiological field for BI-RADS3 category encompasses the circumscribed palpable lesions, complicated cysts and cluster microcysts. The prevalence of various histological findings showed that the most commonly found are atypical ductal hyperplasia, flat epithelial atypia, lobular neoplasia, papillary changes and radial scarring. Histology after the excision points to the higher fre-

quency of benign than malignant changes (74 *vs.* 26 %).[13–16] The alternative approach to these lesions is its removal by VAB technique, in order to avoid the open surgical excision due to the significant number of benign lesions. B3 category was presented in 1.59 % of all cases in our institution. Even though CNB is less specific in differentiating phyllodes tumour from fibroepithelial changes (69.2 %), its specificity is higher than FNAB (21.6 %). This tumour is most commonly described as BI-RADS4 category.[17] Ultrasound is more precise in the detection of phyllodes tumour than mammography, and due to its variations in clinical behaviour, it is appropriate to mark it as B3 lesion.[17] The occurrence of phyllodes tumour among diagnoses in the Centre for Pathology and Histology was 0.32 %. According to the literature, the BI-RADS3 category lesions, identified by ultrasound, present a risk of malignancy <2 %. For these lesions, a close instrumental follow-up every 6 months, then every 6–12 months for 2 years, is suggested in literature.[13–16] A study by Pistolese at al shows that 4.7 % of cases underwent histological verification, and the malignancy rate was 5.7 % – higher than expected.[18] In the 7-year study from USA on 9068 CNB samples, the frequency of benign lesions was 64.2 %, of high-risk lesions 3.5 % and of malignant lesions 32.3 %. After the surgical excision or VAB, the breast carcinoma was confirmed in 3.2 % benign, 26.3 % high-risk and 100 % malignant lesions. In OEB samples, the percentage of underestimated DCIS was 33.6 and 24.5 % for high-risk lesions, such as atypical ductal hyperplasia, flat epithelial atypia and lobular neoplasia.[19] The discordance between radiological and pathohistological diagnoses in the context of benign and malignant nature of breast lesions is particularly noticeable in BI-RADS4 category. Based on our data, 59.97 % of CNB specimens showed no morphological changes or cellular atypia, which leads us to a wide area of biopsy indications in our institution. According to the National Guideline of Good Clinical Practice for diagnosing and treating breast cancer, a biopsy is not indicated in the cases of BI-RADS0-2 category.[16] Within the analysed data, the frequency of these categories further undergoing pathohistological analysis was 5.23 %. The course of core needle biopsy requires a good communication and the accordance between the radiologist, surgeon and pathologist. The specialists in the field of radiology are following BI-RADS system since 2003, which is established on the risk assessment for malignant lesions considering the perennial comparison of numerous imaging findings.[17] Even though there are frequent discrepancies between the radiological and the pathohistological findings, invasive and more expensive surgical procedure and possible complications are generally avoided by histologically defining the benign nature of breast lesions. It is recommended to revise BI-RADS2 category in case of a malignant pathohistological features – B5, in order to avoid overlooking significant breast changes.[16–19] The pathohistological diagnosis is always a definite confirmation of a breast lesion and it has cardinal contribution to the evaluation of CNB qual-

ity. The computer modelling of breast carcinoma represents a new trend in diagnosing breast lesions, which is based on mathematical functions – the artificial neurons. The computer-aided diagnosis was presented in a 2018 study, which showed the relation between mammographic and pathohistological phenotypes and revealed a new model of diagnostic approach: the mammography-histology phenotype, a binding model that allows mapping and connecting the mammographic features with the pathohistological presentation of breast lesions. The reduced unnecessary indications for the biopsy contribution to a simpler and a more accurate clinical decision making about the prognosis and a further clinical approach is expected. The expectations reach the ability of identifying the subcellular models of the expressed genes characteristic of cancer and non-cancer cells, determining the factors responsible for the high-grade lesions, modelling the time progression of first-appearing change, the better prediction of lesion aggressiveness and the possible outcomes for patients.[20] For the purpose of prosper in automatic, digital classification of the verified changes by H&E method, the grand challenge on breast cancer histology images (a BACH challenge) was set and the main goal was to classify and localize the histologically relevant categories based on a large amount of data grouped and published in a specific way.[21]

CONCLUSION

The following is included:

1. The breast cancer is the most common female malignancy in both the developing and developed world and is the primary cause of death among women globally. The risk of breast cancer increases with age and it is assumed that the number of older women living with breast cancer will quadruple by 2040.

2. The core needle biopsy (CNB) is the preferred pathological method for breast cancer diagnosis, compared to the fine-needle aspiration cytology or the surgical excision. The tissue obtained by CNB gives the information regarding the tumour type, the grade and the expression of biomarkers, if needed.

3. Discrepancies between the radiological and the pathohistological findings are frequent, but invasive and more expensive surgical procedure and possible complications can be generally avoided by the histologically defining benign nature of breast lesions.

ИЗВОД

СЕДМОГОДИШЊЕ ИСКУСТВО СА ИГЛЕНИМ БИОПСИЈАМА ЛЕЗИЈА ДОЈКЕ: КОРЕЛАЦИЈА ИЗМЕЂУ ИМИЦИНГА И ХЕМАТОКСИЛИН–ЕОЗИН БОЈЕНИХ ПРЕПАРАТА

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Мамографија представља радиолошку процедуру која омогућава детекцију карцинома дојке у раној фази. BI-RADS систем класификације је детерминисао шест радиолошких категорија за опис лезија присутних у дојци. Иглена биопсија је минимално инвазивна процедура која омогућава добијање узорака за микроскопску анализу, који су надаље подељени у пет група према Б систему класификације. Циљ студије био је сагледање спектра патохистолошких дијагноза, дефинисање најчешће BI-RADS и Б категорије у различитим добним групама и детерминисање заступљености хистолошких дијагноза у различитим BI-RADS категоријама. Студија је обухватила 631 пацијента и подаци су анализирани у односу на локализацију лезије, радиолошке категорије и хистолошке дијагнозе. У свакој добној групи, налаз везан за висок ризик од малигнитета је био најзаступљенији (>2 %). Највећи проценат малигне категорије је био заступљен код пацијенткиња старијих од 61 годину. Крајње дијагнозе показале су девијацију у односу на радиолошку категорију, посебно у категорији BI-RADS 4. Патохистолошка дијагноза је једина дефинитивна потврда типа лезије дојке и има огроман допринос у евалуацији квалитета иглених биопсија.

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