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Radiological diagnostics of triple negative breast cancer: a review

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Background. Triple negative breast cancer has a poor prognosis. Therefore, it is vital to detect this subtype of breast cancer in its early stage. The imaging features of this clinically important subtype of breast cancer are not well known. There have been no published reports about radiological diagnostics of triple negative breast tumour in Lithuania. The purpose of this study was to review the imaging characteristics of triple receptor negative cancers in mammography, ultrasonography and magnetic resonance imaging (MRI).

Materials and methods. The published data for the period 2006–2011 concerning the imaging of triple negative breast cancer were analyzed. There were ten retrospective, ten prospective studies and five reviews. Five studies were on mammography imaging, three on both mammography and ultrasonography imaging, and five studies dealt with MR imaging data. Two studies analysed all three diagnostic methods.

Results. In mammography, triple negative breast (TRN) cancers often present as a mass and are most frequently round, oval or lobular in shape, less frequently being irregular. TRN tumours aren't associated with calcifications. Moreover, architectural distortion is not a characteristic feature of triple negative breast cancer.

In ultrasonography, TRN cancer appears as a parallel. TRN breast tumours mostly are irregular in shape and have a circumscribed margin. Attenuating posterior echoes and hypervascularity are not their characteristic features.

In MR imaging, TRN breast cancer tends to have a lobulated, round or oval mass shape. Rim enhancement is identified in most of TRN tumours. Initially, rapid enhancement with a washout pattern (a sign of malignancy) does not usually apply to triple-negative breast cancers.

Conclusions. TRN breast cancer is difficult to diagnose, because usually it has no specific imaging signs typical of breast cancer. In mammography, TRN cancers aren't associated with microcalcifications. In ultrasonography, attenuating posterior echoes and hypervascularity are not characteristic features of TRN tumours. In MRI, initially rapid enhancement with a washout pattern does not usually apply to triple-negative breast cancers.

Key words: triple negative breast cancer, mammography, ultrasonography, magnetic resonance imaging

INTRODUCTION

Breast cancer is a heterogenic disease. Human breast tumours are histologically complex and have some main gene expression profiles that are likely related to different molecular features of mammary epithelium. Recently, the use of microarray profiling of invasive breast cancer has identified five distinct subtypes of morphologicall similar tumours: luminal A, luminal B, normal breast-like, human epidermal growth factor receptor 2 (HER2) overexpressing, and basal-like (1). The basal-like subtype is characterized by negativity for estrogen receptor (ER), progesterone receptor (PR) and HER2 (1).

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It is important to clarify the relationship between triple receptor negative (TRN) breast cancer and the basal-like phenotype. TRN breast cancer is a term based on clinical assays for ER, PR and HER2, whereas the basal-like phenotype is a molecular phenotype initially defined using cDNA microarrays. Although most TRN breast tumours do cluster within the basal-like subgroup, these terms are not synonymous (2). It should be noted that only about 85% of triple-negative phenotypic breast cancers are deemed to be basal-like when tested by appropriate immunohistochemical methods (3).

The main characteristics of triple-negative cancers in the literature illustrate the similarities between basal-like and triple-negative tumors, including the fact that they more frequently affect younger patients (<50 years), are more prevalent in African-American women, often present as interval cancers and are significantly more aggressive than tumours pertaining to other molecular subgroups (4). Bauer et al. (3) also state that TRN cancer affects younger patients, but they show different age (<40 years) at presentation. They (3) found that a relative survival for women with triple-negative breast cancer was poorer than for women with other types of breast cancer, with 77% of women surviving 5 years after diagnosis versus 93% for other breast cancers. In the study by Rakha (5), the triple negative phenotype was associated with the development of recurrence and distant metastases, and a poorer Nottingham Prognostic Index. It also showed a specific pattern of distant metastases with a high frequency of spinal cord and meninges, brain, liver, and lung metastases. No association was found with the lymph node status (5).

Reis-Filko and Tutt (4) have noticed that triple-negative cancers account for 10–17% of all breast carcinomas, depending on the thresholds used to define ER and PR positivity and the methods for HER2 assessment. Chen et al. (6) found out bigger numbers where TRN cancers account for 12–26% of all types of breast cancers. In the USA, Wei-Tse Yang et al. (7) identified 198 premenopausal women aged 45 years or less who had been diagnosed with primary breast cancer; 38 (19%) women had TRN tumours. Dent et al. (8) determined 180 triple-negative breast cancers from 1.601 patients (11.2%). So, with reference to various authors, the relevance of triple negative breast cancer is 10–26%.

Although mammography is the gold standard for breast cancer screening, clinical breast examination (CBE) and breast self-examination (BSE) are important adjuncts whose utility has been questioned (28). Haakinson et al. (9) found out that patients presenting with palpable masses on SBE or CBE, even with a normal mammogram, within one year tended to have more aggressive tumours (larger size, lymph node positive, and triple-negative disease) resulting in a more aggressive therapy (a higher mastectomy rate and a greater likelihood of chemotherapy).

To detect the triple-negative subtype of breast cancer in its early stage is vital. The imaging features of this clinically important subtype of tumour are not well known. To our knowledge, there have been no published reports about the imaging of triple negative breast cancer (mammography, ultrasonography, magnetic resonance imaging) in Lithuania. So, the purpose of this study was to review the imaging characteristics of these cancers on mammography, ultrasonography and magnetic resonance imaging.

RADIOLOGICAL DIAGNOSTICS OF TRIPLE NEGATIVE BREAST CANCER

Current screening modalities for triple negative breast cancer diagnosis include mammography, ultrasonography, magnetic resonance imaging and other methods of diagnostics (positron emission tomography, molecular breast imaging).

Dent et al. (8) compared the proportions of breast cancers discovered initially by imaging (mammography or ultrasonography) and by clinical detection (clinician or patient). Because screening mammography is routinely recommended for all women in Ontario after the age of 50, they restricted this analysis to women diagnosed at age ≥50. Patients with triple negative breast tumours had a much lower proportion of breast cancers first detected by mammography or ultrasonography than patients with other breast cancers (19.6% versus 36.0%; $p = 0.0008$).

Mammographic features

There are not so many studies describing mammography findings of triple negative breast cancer. The mammographic findings of Yang et al. (7) reflect the biologic differences that exist among immunophenotypes of breast tumor and indicate that TRN cancer is a distinct clinical entity. Its combined mammographic and pathologic features suggest a more rapid pattern of carcinogenesis, which leads directly to invasive cancer, with no major *in situ* component or precancerous stage (7).

Various authors analyze such imaging features of mammography as focal asymmetry, breast density, visibility, mass, calcification, architectural distortion, mass shape and margin. All of them will be reviewed.

Focal asymmetries

In the study by Ko et al. (1), most triple negative breast cancers were seen as focal asymmetry (19/87, 22%), whereas only 4 out of 65 (6%) ER-negative / PR-negative / HER2-positive (HER2+) and 7 out of 93 (8%) ER-positive / PR-negative / HER2-negative (ER+) tumours were seen as focal asymmetry ($p = 0.0030$). Another study, which analyzed features of only TRN breast cancer (10), found similar results on focal asymmetry between them (20.9%, 9/43). However,

in one study (11) authors noted that TRN cancers were less associated with focal asymmetric density (8/85, 9.4%).

Density

Domingo et al. (12) identified that in mammograms high breast density and triple negative phenotype were more frequent in true interval cancers than in screen-detected cancers, while no statistically significant differences were observed between false negative and screen-detected cancers. The main adjusted factors associated with true interval cancers compared with screen-detected cancers were high breast density and triple negative phenotype.

In the study by Yang et al. (7), mammographic density was similar between all immunophenotypes of tumours. All of them were most frequently associated with type 3. Another study, analyzing features of only TRN cancer, showed very similar proportions in the types of breast density (Table 1).

Ma et al. (13) found no difference in the association of percent mammographic density with luminal A and triple negative breast cancer. Percent mammographic density was positively associated with both luminal A and triple-negative tumours. Further, the effect of modification on these two subtypes was statistically significant neither by race nor by menopausal status. The associations were similar when restricted to nulliparous and parous women separately (13).

Visibility

In the study by Dogan et al. (10), TRN cancers were visible on 39 (90.7%) of 43 mammograms. Yang et al. (7) noticed that mammographic tumour visibility was similar among all immunophenotypes. The difference was not statistically significant, but it may be useful to mention that the part of not visible tumour was biggest in the TRN cancer group (5/38, 13%), while in the HER2+ group it was 3 out of 67 (5%) and in the ER+ group 6 out of 93 (7%).

Mass

Yang et al. (7) found that TRN cancers most commonly presented as a mass in mammography (28/38, 85%). In the study by Ko et al. (1), most of triple negative tumours were seen as a mass compared with ER+ and HER2+ breast cancers (43/87, 49% compared with 42/93, 45% and 7/65, 11%). Kojima and Tsunoda (11) have concluded that triple negative breast cancer often presents as a mass (62.4%) in mammography. The same observation was established by Dogan et al. (10) (Table 2).

Calcifications

Yang et al. (7) noticed that TRN cancers weren't associated with microcalcifications; irregular spiculated masses and pleomorphic microcalcifications, which are typical malignancy features, were not usually apparent. In the study by Ko et al. (1), triple negative tumours were less likely to have an associated calcification compared with ER+ and HER2+, the difference being statistically significant. In particular, HER2+ breast cancers were more likely to be associated with calcifications. A study which analyzed only TRN cancers (11) found that this type appeared as calcifications only in 10 out of 85 (11.8%) cases. Another study (10) proposed somewhat lower numbers – 3 out of 43 (7%) (Table 2).

The lack of mammographic microcalcifications is concordant with the low incidence of associated ductal carcinoma *in situ* in TRN carcinomas (7). It reflects the biological differences that exist among breast tumour phenotypes and indicates that triple negative breast cancer is a distinct clinical entity. According to these investigators, the combined mammographic and pathological features of this cancer suggest a more rapid pattern of carcinogenesis that leads directly to invasive cancer, with no major *in situ* component or precancerous stage (1).

Wang et al. (14) determined that the osteopontin (OPN-secreted glycoprotein) could play a role in the formation of calcifications which are often associated with breast cancer. Authors found that calcifications of the triple negative phenotype on mammograms were significantly associated with the OPN status. In contrast to OPN-negative tumours, OPN-positive tumours were more likely to have spiculated margins (57.6% versus 9.2%), to be associated with calcifications (54.3% versus 30.6%), to be of a triple negative phenotype (26% versus 8.1%), and to have axillary lymph node metastases (81.5% versus 38.8%). Most calcifications were of pleomorphic morphology (60.4% versus 11.8%, $p = 0.046$).

Table 1. **Mammographic density among patients with TRN, HER2+ and ER+ breast cancers in two studies**

Authors of the study	Yang et al. (7)			Kojima and Tsunoda (11)
Immunophenotype of breast cancer / Breast density (ACR BI-RADS classification)	TRN (n = 38)	HER2+ (n = 67)	ER+ (n = 93)	TRN (n = 85)
1	1 (3%)	0	1 (1%)	3 (3.5%)
2	5 (13%)	7 (10%)	15 (16%)	35 (41.2%)
3	25 (66%)	41 (61%)	64 (69%)	43 (50.6%)
4	7 (18%)	19 (28%)	13 (14%)	4 (4.7%)

Table 2. **Mass, calcification, mass + calcifications and architectural distortion among TRN, HER2+, ER+ groups of breast cancer in several trials**

Feature \ Authors of the trial	Yang et al. (7) (n = 198) *1			Ko et al. (1) (n = 245)			Kojima and Tsunoda (11) (n = 85)		Dogan et al. (10) (n = 43)	
	Immunophenotype		p value	Immunophenotype		p value	Immunophenotype		Immunophenotype	
Number of patients	TRN	33 (87%)		TRN	87 (35.5%)		TRN	85	TRN	43
	HER2+	64 (96%)		HER2+	65 (26.5%)					
	ER+	87 (94%)		ER+	93 (38%)					
Mass only	TRN	28 (85%)	<0.0001	TRN	43 (49%)	<0.0001	2 TRN	53 (62.4%)	TRN	23 (53.5%)
	HER2+	11 (17%)		HER2+	7 (11%)					
	ER+	15 (17%)		ER+	42 (45%)					
Calcification only	TRN	0	0.001	TRN	6 (7%)	<0.0001	TRN	10 (11.8%)	TRN	3 (7%)
	HER2+	19 (30%)		HER2+	23 (35%)					
	ER+	26 (30%)		ER+	12 (13%)					
Mass + calcifications	TRN	5 (15%)	0.071	TRN	18 (21%)	0.0055	TRN	11 (20.8%)	TRN	2 (4.7%)
	HER2+	24 (38%)		HER2+	29 (45%)					
	ER+	27 (31%)		ER+	26 (28%)					
Architectural distortion	TRN	0	0.003	TRN	1 (1%)	0.4797	TRN	6 (7%)	TRN	2 (4.7%)
	HER2+	10 (16%)		HER2+	0					
	ER+	23 (26%)		ER+	2 (2%)					

*1 – in this study, mass, calcification, mass + calcifications and architectural distortion were analyzed among patients with visible tumours only. Therefore, here we give the numbers of patients with visible tumour. The numbers of patients with visible and non-visible tumours together are: TRN 38 (19%), HER2 67 (34%) and ER+ 93 (47%).

Mass shape

It is known that irregular shape and spiculated margins are both typical features of malignancy (7). In the study by Yand et al. (7), TRN cancers that appeared as masses were most frequently round, oval or lobular in shape, with indistinct margins. They less frequently irregular in shape (8/33, 24%) than HER2+ (22/35, 63%) and ER+ (21/42, 50%) cancers and were less likely to have spiculated margins (6/33, 18%) than were HER2+ (18/35, 51%) and ER+ (25/42, 60%) cancers. In the study by Dogan et al. (10), 15 (60%) of the 25 masses were round or oval.

Mass margin

In the study by Kojima and Tsunoda (11), TRN breast tumours presenting as masses most frequently showed microlobulated margins (21/53, 39.6%), indistinct margins (17/53, 32.0%) and circumscribed margins (11/53, 20.8%). Spiculated margins, so common for malignancy, were rare (4/53, 7.5%). Another study showed different results. Yand et al. (7) identified indistinct margins as the most frequent type of margin among patients with visible tumours only (15/33, 45%). Circumscribed (8/33, 24%), spiculated (6/33, 18%), obscured (4/33, 12%) margins were rarer, and microlobulated margins were not identified in the group of TRN tumours. In HER2+ and ER+ groups the results were opposite (Table 3). In the study by Dogan et al. (10), eight of 25 TRN tumour masses (32%) had circumscribed margins.

Ultrasonography

Combined mammography or ultrasound imaging findings of a non-calcified mass that is seen as a markedly hypoechoic mass with a circumscribed margin can be used to predict the presence of triple-negative breast cancer (1). Although this tumour can mimic a lesion with a benign morphology, its mammographic or ultrasound imaging recognition can assist in both the pretreatment planning and prognosis as well as contribute to a better understanding of the biological behaviour of the disease entity (1).

Kojima and Tsunoda (11) identified a small number of patients (according to their mammograms) who were diagnosed with cancer without any abnormalities on mammography. If this happens in a normal screening process, such patients might slip through undiagnosed. Authors noted that ultrasound did indeed pick up all abnormalities. As a result, they concluded that ultrasound used in combination with mammography is advantageous in detecting triple negative cancer. Mammography and ultrasound imaging together have shown that the morphological features of triple negative tumour include a lobulated mass, with less attenuating posterior echoes, some vascularity, and low elasticity (11). Despite their large size at presentation, triple receptor negative cancers may be occult in mammography or sonography and frequently have benign or indeterminate features (10). Wang et al. (15) compared the mammographic and ultrasonographic findings of ER-negative / HER2-negative cancers with those of ER-negative / HER2-positive cancers and

Table 3. **Incidence of different types of mass margins among patients with TRN, HER2+ or ER+ breast cancers**

Authors of the study	Yang et al. (7) *1			Kojima and Tsunoda (11)
Immunophenotype of breast cancer / Mass margin	TRN (n = 38, visible n = 33)	HER2+ (n = 67, visible n = 64)	ER+ (n = 93, visible n = 87)	TRN (n = 53)
Circumscribed	8 (24%)	0	0	11 (20.8%)
Obscured	4 (12%)	2 (6%)	1 (2%)	– *2
Microlobulated	0	3 (9%)	0	21 (39.6%)
Indistinct	15 (45%)	12 (34%)	16 (38%)	17 (32 %)
Spiculated	6 (18%)	18 (51%)	25 (60%)	4 (7.5%)

*1 – in this study, different types of mass margin were analyzed among patients with visible tumours only.

*2 – in this study no such type of margin was noted.

concluded that ER-negative / HER2-positive tumours were likely to have spiculated margins and to be associated with calcifications. In addition, ER-negative / HER2-negative tumours were more likely to appear as smooth or circumscribed masses (15). The basal-like subtype is strongly associated with the presence of a central scar, tumour necrosis, spindle cells or squamous metaplasia, a high total mitotic count and a high nuclear-cytoplasmic ratio. Consequently, mammography and ultrasonography could reveal a smooth border in ER-negative / HER2-negative breast cancers; however, it might be difficult for these conventional breast imaging methods to reveal the intratumoral characteristics, such as necrosis and fibrosis, in this particular subtype (15).

Masses

In three studies (1, 10, 11), on ultrasonography more than 85% TRN breast cancer patients presented with masses.

In the study by Ko et al. (1), on ultrasonography, 75 out of 87 (86%) triple-negative tumour patients presented with masses. ER+ breast cancer showed a similar pattern. However, for HER2+ subtype, 21 out of 65 (32%) tumours were seen with non-mass lesions. Dogan et al. (10) found that 38 (86%) of 44 cancers appeared as masses. In a study by Kojima and Tsunoda (11), on ultrasonography, 74 out of 80 (92.5%) triple negative breast cancer patients presented with masses.

Posterior echoes

In a study when patients with triple negative tumour were retrospectively reviewed (11), on ultrasound, 40 out of 80 (50%) had no change, less cancers (33/80, 41.3%) had accentuating posterior echoes, and only several of them (7/80, 8.7%) showed attenuating posterior echoes. In another study (10), posterior acoustic enhancement was identified in nine (23.7%) of the masses.

Ko et al. (1) ascertained differences of posterior echoes between the TRN, ER+ and HER2+ groups. The highest percentages of accentuating posterior echoes were found in the HER2+ and TRN groups (22/44, 50% and 37/75, 49%). In the ER+ group, 40 out of 78 (51%) cancers showed no change in posterior echoes. In the TRN group, the numbers were somewhat less (43/75, 45%) and in the HER2+ group even more less (16/44, 36%). Analyzing the attenuating posterior echoes in a study by Ko et al. (1), we saw that this feature was least frequent in TRN tumour (4/75, 5%). In the HER2+ group it was found in 6 out of 44 (14%) cancers and in the ER+ group in 15 out of 78 (19%). Posterior shadowing was least common in triple negative breast cancers as compared with the other two types of lesions (1).

Vascularity

This feature was analyzed by Kojima and Tsunoda (11). Hypervascularity was identified in 10 out of 80 (12.5%) TRN cancers, avascularity in 8 out of 80 (10%), spotty signals in 29 out of 80 (36.3%), and hypovascularity composed the biggest part (33/80, 41.2%).

Elasticity score

In the study by Kojima and Tsunoda (11), among the patients who were able to have elastography, triple-negative tumours appeared as hard masses, with elasticity scores of 4 or 5. Such elasticity score of triple-negative tumour is as high as that of ordinary invasive ductal carcinoma (11).

Shape of mass

In the study by Ko et al. (1), triple-negative breast cancers were usually irregular (87%) in shape, as were also the other two types of cancers. Notably, these tumours more frequently had an oval shape (16%).

Margin

Ko et al. (1) found that TRN usually had a circumscribed margin (43/87, 57%), whereas ER+ and HER2+ commonly had an angular margin (28/93, 36% and 14/65, 32%). In the study by Dogan et al. (10), margins were circumscribed in eight (21.1%) of 38 masses.

Lesion boundary

Anbrupt interface was characteristic of the majority of TRN, ER+ and HER2+ cancers (1).

Orientation

Orientation is evaluated according to skin (parallel or not parallel to skin). For TRN cancer, the most common orientation is parallel (1). Parallel orientation is more characteristic of a benign process. TRN cancer appears as parallel, and this feature impedes its diagnostics.

MR imaging findings

In contrast to mammography, magnetic resonance (MR) imaging yields important information not only on the morphology of benign and malignant lesions of the breast, but also on the functional aspects reflected by the temporal and spatial uptake of contrast medium. This enhancement is influenced by the extent and pattern of vascularization, vessel permeability, cellularity, interstitial pressure, and the fraction of the extracellular space (16).

MR findings of a unifocal lesion, mass lesion type, smooth mass margin, rim heterogeneous enhancement, persistent enhancement pattern, and a very high signal intensity on T2-weighted images are typical features of breast MR imaging associated with TRN breast cancer. Although it can mimic a benign morphology, its early MR imaging recognition could assist in both the pretreatment planning and the prognosis, as well as add to our understanding of its biological behaviour (17). Uematsu's et al. (18) conclusion: several MR imaging features might be used for detecting triple negative breast cancer. Their study results have shown that several MR imaging findings, such as mass lesion type, smooth mass margin, rim enhancement, persistent enhancement pattern, and intratumoral necrosis, are suggestive of histopathologically triple negative breast cancer. Their study has shown that several MR imaging findings can be used for detecting this cancer. However, breast MR imaging with imperfect positive and negative predictive values cannot replace tissue sampling (18). Loo et al. (19) have established that MR imaging during neoadjuvant chemotherapy (NAC) to monitor response is effective in triple-negative or HER2-positive disease but is inaccurate in ER-positive / HER2-negative breast cancer.

Lesion

Uematsu et al. (18) noted that unifocal lesions were significantly associated with triple negative breast cancer in comparison with ER-positive / PR-positive / HER2-negative (HER2-). For triple negative breast cancers, 39 out of 59 lesions (66%) were of the unifocal type, 20 out of 59 (34%) were multifocal, and none was of the multicentric type.

Mass

Three studies have shown that TRN tumour most often presents as mass enhancement and less commonly as non-mass-like enhancement (Table 4). In the study by Chen et al. (6), except for one patient presenting with a non-mass type of regional enhancement, the other 28 patients (97%) had mass-type lesions. Twenty-six of the 28 mass-type lesions (93%) were >1.5 cm and showed strong and / or heterogeneous enhancements. Uematsu et al. (18) gave a very similar distribution of mass-type and non-mass type lesions in the TRN group (95% and 5%). In the third study (6), the percentages were somewhat different, but we can see the same tendency: TRN usually appeared as a mass-type lesion (77.3%).

Shape

TRN breast cancer tended to have a lobulated, round or oval mass shape. In the study by Dogan et al. (10), it most commonly had a round or oval shape (16/34, 47%). Other types of shape were rarer (lobulated 14/34, 41%, irregular 4/34, 12%). In another study (18), the round or oval and lobulated shapes had a similar frequency (41%), and the irregular shape was rarer (10/56, 18%). As to mass shape, TNBC tends to have a benign mass shape, although mass shape is not very important for differentiating malignancy from benignancy (17).

Rim

In the study by Chen et al. (6), rim enhancement, a specific sign of malignancy on breast MR imaging, was identified in 12 patients (41%). Two other studies (10, 18) mentioned not only rim enhancement, but also other types of internal enhancement, such as homogeneous and heterogeneous. In both studies the tendency was the same: the majority were TRN cancers with rim enhancement (80% and 76.5%), and a less part comprised cancers with heterogeneous enhancement (20% and 17.6%). In the first study no homogeneous enhancement was found, and in the second study it made the least part of all types of enhancement (5.9%).

Table 4. **Mass-type and non-mass-type lesions of TRN and HER- breast cancers in three studies**

Magnetic resonance morphology \ Authors of the study	Uematsu et al. (18) (TRN n = 59, HER- n = 117)		Chen et al. (6) (n = 29)		Dogan et al. (10) (n = 44)	
	Immunophenotype		Immunophenotype		Immunophenotype	
Mass-type lesion	TRN HER-	56 (95%) 78 (66.7%)	TRN	28 (97%)	TRN	34 (77.3%)
Non-mass-type lesion	TRN HER-	3 (5%) 39 (33.4%)	TRN	1 (3%)	TRN	10 (22.7%)

Margin

Uematsu et al. (18) reported that the majority of TRN tumours were of mass lesion type on MR imaging (95%), and of the 56 mass lesions studied, 61% had an irregular and 39% a smooth mass margin. In another study (10), the numbers are almost identical: 61.8% (21/34) had an irregular and 38.2% (13/34) a smooth mass margin. The smooth mass margin tended to be associated with TRN breast cancer. This is important because a smooth border of a mass is frequently used as indicative of a benign lesion. High-grade tumours, such as triple negative and familial breast cancer, are likely to manifest benign morphologic features (17).

Intratumoral signal intensity on T2-weighted images

In the study by Uematsu et al. (18), a very high intratumoral signal intensity on T2-weighted MR images was significantly associated with triple negative breast cancer.

Enhancement features

Uematsu et al. (18) reported that for the time–signal intensity curve pattern, a persistent enhancement pattern was significantly associated with TRN breast cancer. The initially rapid enhancement with a washout pattern is generally regarded to be a malignant pattern at breast MR imaging; however, this does not apply to triple-negative breast cancers. This different enhancement pattern may stem from the heterogeneity of triple-negative tumour, because this cancer showed no homogeneous internal enhancement in their study. In the study by Schrading and Kuhl (20), a high percentage (33%, 25/76) of familial breast cancer exhibited benign kinetic features. These results suggest that highgrade tumour is likely to manifest with benign kinetic features (18). In the study by Chen et al. (6) 22 lesions had documented enhancement kinetic curves, and all showed a typical malignant kinetic feature with a rapid up-slope followed by washout (100%). The morphological and kinetics features are in accordance with MRI features of invasive ductal carcinoma.

In the study by Dogan et al. (10), a time-intensity analysis revealed type 3 (i. e. a fast initial upstroke followed by early intensity loss, or washout) in 40 (91%) of 44 TRN tumours. The other four cancers showed a progressive or plateau-type time-intensity curve.

Li et al. (21) have ascertained TRN breast cancer to possess characteristic features on imaging, with a lower extracellular space (higher cell density) and a higher contrast agent wash-out rate (higher vascular permeability), suggesting a distinctive phenotype detectable by MRI.

Lymph nodes

In the study by Chen et al. (6), fourteen patients (14/29, 48%) showed identifiable lymph nodes in the axillary region. Uematsu et al. (18) compared TRN and HER2-, their axillary lymph node positivity. Their results: 21 out of 59 (36%) TRN and 45 out of 117 (38.5%) HER2- cancers were axillary lymph node positive. It was reported that in TRN and non-TRN tumours with the same positive nodal status, the 5-year nodal relapse-free rate was significantly different between the two groups, and the TRN subtype was more frequently associated with a higher pathologic stage of the nodal status than the non-TRN subtype (6).

Other methods

Positron emission tomography

Basu's et al. (22) study was designed to investigate the fluorine-18 fluorodeoxyglucose (FDG)-positron emission tomography (PET) imaging characteristics of triple-negative breast carcinoma and to compare the results with characteristics of HER2- breast carcinomas which usually carry a favourable prognosis. Their conclusion was as follows: triple-negative breast tumors were associated with enhanced FDG uptake commensurate with their aggressive biology and were detected with a very high sensitivity by using FDG-PET imaging. For these cancers, the sensitivity of PET for detecting a lesion in their population was 100%. Basu et al. (22) proposed that FDG-PET imaging may be a useful technique for measuring tumour activity and treatment response in therapy development.

Specht et al. (23) write that dynamic PET imaging can identify patterns of breast cancer metabolism and perfusion in patients receiving NAC that are predictive of response. Results of their study: the metabolic rate (MRFDG) for TRN tumours was on average by 67% higher than for luminal tumours, and the average MRFDG / BF ratio was by 53% greater in TRN as compared with luminal tumours. They conclude that the relationship between breast tumour metabolism and perfusion differ by subtype. The high MRFDG / BF ratio that predicts a poor response to NAC was more common in TRN tumours. Metabolism and perfusion measures may identify subsets of tumours both susceptible and resistant to NAC and may help direct targeted therapy.

Molecular breast imaging

O'Connor et al. (24) write that molecular breast imaging (MBI) is a new nuclear medicine technique that employs small semiconductor γ-cameras for high-resolution imaging of the breast. The imaging technique is similar to mammography but only uses the compression force. They report the early results to indicate that MBI has a comparable sensitivity to breast MRI, but at a fraction of the cost per procedure. In a screening study of women with a dense breast tissue at an increased risk of breast cancer, MBI detected three times as many tumours as did mammography while maintaining a lower false-positive rate. The goal of the recent work is to reduce the effective dose to the level of screening mammography (24).

CONCLUSIONS

With reference to various authors, the relevance of triple receptor negative breast cancer is 10–26%. This cancer is difficult to diagnose, because sometimes it has no specific imaging signs usual in breast cancer.

1. In mammography, usually about one fifth of triple negative breast cancers present as focal asymmetry. Not all cases of triple negative tumours are visible on mammograms, it often presents as a mass. TRN cancers that appear as masses are most frequently round, oval or lobular in shape. Often tumours have indistinct margins. TRN cancers aren't associated with calcifications. Architectural distortion isn't their characteristic feature. Identification of TRN cancer is complicated on mammograms because it usually hasn't typical malignant features, such as microcalcifications, irregular shape and spiculated margins.

2. In ultrasonography, most of TRN breast cancers present as masses. Under half of them have accentuating posterior echoes. Only several of TRN tumours show attenuating posterior echoes. Hypervascularity isn't a characteristic feature of these tumors. TRN breast cancer appears as hard masses, with elasticity scores of 4 or 5 on elastography images. TRN cancers usually appear as a parallel-oriented mass, a feature more characteristic of a benign process. TRN breast cancers are mostly irregular in shape and have a circumscribed margin.

3. On MR imaging, TRN cancers more often present as unifocal lesions than HER2- cancers. TRN tumour most often presents as a mass enhancement. Usually, it has a lobulated, round or oval mass shape. Rim enhancement, a specific sign of malignancy on breast MR imaging, is identified in the majority of these tumours. Usually tumours present with an irregular mass margin, but sometimes a smooth mass margin is visualised. This is important because a smooth border of a mass is frequently considered being indicative of a benign lesion. A very high intratumoral signal intensity on T2-weighted MR images is associated with triple negative breast cancer. The initially rapid enhancement with a washout pattern (a sign of malignancy) does not usually match with the TRN cancer type. The TRN subtype is more frequently associated with a higher pathologic stage of the nodal status than the non-TRN subtype.

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TRIGUBAI NEIGIAMO KRŪTIES VĖŽIO RADIOLOGINĖ DIAGNOSTIKA (APŽVALGA)

Santrauka

Įvadas. Trigubai neigiamas krūties vėžys (TNKV) pasižymi bloga prognoze, todėl yra gyvybiškai svarbu aptikti šį krūties vėžio tipą ankstyvos stadijos. Šio kliniškai svarbaus tipo radiologiniai požymiai nėra gerai žinomi. Lietuvoje nėra paskelbta mokslinių straipsnių apie TNKV radiologinę diagnostiką. Šio straipsnio tikslas yra apžvelgti TNKV radiologinius – mamografinius, ultrasonografinius ir magnetinio rezonanso – požymius.

Metodai. Tarp analizuotų 2006–2011 metų publikacijų apie TNKV buvo 10 retrospektyvinių studijų, 10 prospektyvinių ir 5 apžvalgos. Apie mamografiją buvo rašoma penkiose studijose, apie mamografiją ir ultrasonografiją – trijose, apie magnetinio rezonanso tomografiją – penkiose. Dviejose studijose buvo analizuojami visų tyrimo metodų požymiai.

Rezultatai. Mamografiškai TNKV dažniausiai matomas kaip apvalus, ovalus arba skiltėtos formos darinys, rečiau – netaisyklingas, nesusijęs su mikrokalcinatais. Be to, jam nebūdinga parenchimos deformacija.

Ultrasonografiškai TNKV matomas paralelinėje orientacijoje, dažniausiai yra netaisyklingos formos, su aiškiomis ribomis. Jam nebūdingas susilpnėjęs užpakalinis echogeniškumas ir vaskuliarizacija.

Tiriant magnetinio rezonanso tomografija, TNKV matomi kaip skiltėti, apvalūs ar ovalūs dariniai, daugeliui jų būdingas išryškėjęs kraštas. Ankstyvas ir greitas kontrasto kaupimas ir greitas „išsiplovimas" (įprastas piktybiškumo požymis) nėra būdingas TNKV.

Išvados. Trigubai neigiamą krūties vėžį diagnozuoti yra sunku, nes jis neretai neturi specifinių radiologinių požymių, būdingų krūties vėžiui: tiriant mamografiškai, TNKV nesusijęs su mikrokalcinatais, ultrasonografiškai – jam nebūdingas susilpnėjęs užpakalinis echogeniškumas ir vaskuliarizacija, tiriant magnetinio rezonanso tomografija, nėra būdinga piktybinio kontrastavimo kreivė.

Raktažodžiai: trigubai neigiamas krūties vėžys, mamografija, ultrasonografija, magnetinio rezonanso tomografija