Original Article Archive of SID Agreement of Breast Nodularity on Clinical Examination and Mammographic Density

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Background: Breast density is routinely reported on mammograms, while breast nodularity is seldom reported on clinical examination, and there is no standard system for its classification. Objectives: The aim of this study was to evaluate the agreement of mammographic density with nodularity on clinical breast examination (CBE). In addition, the relationship of mammographic density with age, menopausal status, and number of parities were assessed. Methods: This cross-sectional study was conducted from September 2013 to February 2014, on 30-70-year-old women who referred for screening or diagnostic mammography to Shahid Beheshti Hospital, Kashan, Iran. Nodule size, nodule consistency, and mammographic density were assessed, and Cohen's kappa coefficient was calculated. The Chi-square test was also used to assess the relationship of mammographic density with age, menopausal status, and a number of parities. **Results:** In this study, 320 women with an age mean value of 46.01 ± 7.73 underwent mammography and CBE. Mammographic density showed a statistically significant weak agreement with nodule size (Kappa coefficient = 0.275; P < 0.001) and nodule consistency (Kappa coefficient = 0.256; P < 0.001). Moreover, mammographic density was inversely related to age, menopausal status, and number of parities (P < 0.001). Conclusions: Breast nodularity on clinical examination has only a weak agreement with mammographic density. Further studies are needed to develop more comprehensive instruments for assessing not only nodule size and consistency but also nodules distribution in all breast quadrants.

Keywords: *Physical examination, Breast density, Mammography, Nodularity, Early detection of cancer*

INTRODUCTION

128

*C*linical breast examination (CBE) is an important step in the evaluation of women with breast complaints. Abnormal findings on inspection and palpation should be precisely defined and recorded. However, there are no standard guidelines for describing and reporting the breast nodularity on the CBE.^[1] Instead, nodules in the breast are often simply called fibrocystic disease, without any exact definition of objective clinical findings such as the size and the consistency of the palpable nodules and their distribution in the breast tissue.^[2]

One of the first attempts for the breast nodularity assessment was made by Haagensen in 1971, who

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developed a scale to assess the nodularity in each breast quadrant.^[3] Ernster *et al.*, other pioneers in breast nodularity classification, also developed a 1–4 scoring system for evaluating nodularity in each breast quadrant.^[4,5] Later, Goodson *et al.* developed a 1–4 ordinal scale to assess breast durity (or hardness) and breast nodularity in the most nodular breast quadrant. They assessed nodularity in the upper

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outer breast quadrant and scored it as follows: (1) no nodularity; (2) fine nodularity (like rice); (3) prominent nodularity (like peas); and (4) coarse nodularity (like beans). Then, to simplify interpretations, they classified scores 1 and 2 as less nodular and scores three and four as more nodular breast.^[6] Finally, Kumar et al. proposed the more user-friendly Lucknow-Cardiff breast nodularity scale, which is a visual analog scale with five schematic pictures representing different nodularity patterns of the breast.^[1,7] Although, the Lucknow-Cardiff breast nodularity scale is a very simple and easy-to-use scale to assess nodularity distribution in the breast, it fails to assess nodularity size and consistency. Due to the importance of the breast consistency, Grady et al. also classified nodules according to their consistency into firm, rubbery, and fluctuant categories.^[2]

Contrary to the lack of standard guidelines for the classification of nodularity on CBE, there are guidelines for the classification of mammographic density. For instance, it is currently for >10 years that radiologists are using the American College of Radiology Breast Density Classification.^[8] Dense breasts on mammography are routinely seen in young women, those receiving estrogen replacement therapy and women with fewer parities.^[9,10] The sensitivity of mammography in detecting breast cancer can be 87% in nondense breasts; however, its sensitivity may be as limited as 48% when the breast is dense because high density may hide some lesions.^[11] Meanwhile, women with dense breasts are at greater risk for breast cancer compared to those with fatty breasts.^[12,13]

Due to the limitations of mammography in women with dense breasts, there is a trend toward using other imaging techniques such as ultrasound or magnetic resonance imaging.^[14-16] Accordingly, women with high density mammogram are usually referred back to radiologists for complementary ultrasound. Frequent postmammography referrals to radiologists may waste time, money, and energy.

To the best of our knowledge, it is still unknown whether nodularity on CBE is related to mammographic density. In other words, it is still unclear whether a doctor should simultaneously request complementary ultrasound in addition to mammography in case of any nodularity on CBE to avoid postmammography request for ultrasound for women with dense breast.

Objectives

The aim of this study was to evaluate the agreement of mammographic density with nodularity on CBE and the relationship of mammographic density with age, menopausal status, and number of parities.

Methods

This cross-sectional study was conducted from September 2013 to February 2014. The study sample consisted of 320 women who referred for screening or diagnostic mammography to Shahid Beheshti Hospital, Kashan, Iran. Sample size was calculated based on the results of a pilot study on thirty women and with P_o , P_e , and density-nodularity agreement of 0.72, 0.5, and 0.45, respectively. Women were included if they were not breastfeeding mothers, had no history of surgery, and had not received hormone replacement therapy in the past 2 years before the study.

Initially, data on each eligible woman's age, menopausal status, and number of parities were gathered. Then, CBE and nodularity assessment were performed by a general surgeon using the Goodson's nodularity scale. The scale assessed nodularity in the breast quadrant with the greatest nodularity on a four-point scale as follows: (1) no nodularity; (2) fine nodularity; (3) prominent nodularity; and (4) coarse nodularity. Then, scores 1 and 2 are classified as less nodular, while scores three and four as more nodular.^[6] Besides, the consistency of nodules was assessed and scored as the following: (1) soft (like adipose tissue) or elastic (like normal lymph nodes); and (2) hard or coarse (like cartilage). Standard analog mammography (Planmed Sophie Co., Finland) was performed for each woman with craniocaudal and mediolateral views and subsequently, mammographic density was determined by a radiologist according to the American College of Radiology Breast Density Classification. The four classes of the classification are as follows: (1) fatty breast with no dense areas; (2) scattered dense areas in <50% of the breast; (3) heterogeneously dense tissue in <75% of the breast; and (4) entirely dense breast with more than 75% dense areas.^[8] Classes one and two were considered as low density and classes three and four as high density. The radiologist was blind to the results of CBE.

Ethical considerations

The study was approved by the Institutional Review Board and the Ethics Committee of Kashan University of Medical Sciences, Kashan, Iran (approval code: 3556; approval data: 15.10.2014). Informed consent was gotten from all women and they were assured data confidentiality. The research team committed to protect participant's rights according to the Declaration of Helsinki.

Data analysis

Cohen's kappa coefficient was calculated to determine the agreement of mammographic density with breast nodularity and consistency on CBE. The relationship

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of mammographic density with age, menopausal status, and number of parities was assessed through the Chi-square test. Data were analyzed using SPSS software version 16 (SPSS INC., Chicago, IL, USA) and P < 0.05 was considered as statistically significant.

RESULTS

A total of 320 women with an age mean value of 46.01 ± 7.73 years were included in the study. Thirty one percent of participants were postmenopausal and 23% had four or more parities [Table 1]. The more nodular pattern was observed in 58.43% of participants (i.e., in 70.9% of women aged <40 and 35% of women aged >50 years) [Table 1]. Regarding the consistency of nodules, 24.37% of participants had hard nodules [Table 2]. High-density mammograms were observed among 47.5% of the participants [Table 1].

Nodularity on CBE showed a weak agreement with mammographic density (Kappa coefficient = 0.275; P < 0.001). However, the Kappa coefficients were somewhat better in women who aged <49 years, premenopausal women, and women with four or more parities [Table 1]. Agreement analysis also showed a weak agreement between mammographic density and nodular consistency on CBE (Kappa coefficient = 0.256; P < 0.001) [Table 2].

The results of the Chi-square test also illustrated the significant relationship of mammographic density

with age, menopausal status, and number of parities [P < 0.001; Table 3].

DISCUSSION

In the present study, breast nodularity and consistency on CBE showed no strong agreement with mammographic breast density. To the best of our knowledge, none of the previous studies examined the relationship of mammographic density with breast nodularity. Of course, a study reported that mammographic density had no significant relationship with postcompression breast thickness.^[17] In another study, Goodson et al. also showed that the results of CBE were not significantly related to high-risk histopathological pattern in breast tissue.^[6] It is worthy to note that Goodson's scale assessed nodularity in only one quadrant of the breast, while mammographic density is assessed based on the surface area of dense breast tissue. This difference between the nodularity and density assessment methods may be an explanation for the weak density-nodularity agreement in the present study. Simultaneous assessment of nodular size (using Goodson's scale), nodular distribution (using Kumar scale), and nodular consistency may provide different and more reliable results.

The findings of the present study also showed the significant relationship of mammographic density with age, postmenopausal status, and number of

Table 1: The agreement of mammographic density with nodular size on clinical breast examination						
Variables	Nodular size	Densit	y, n (%)	к (95% CI)	Р	
		Low	High			
Age (years)						
<40	Less nodular	9 (56.25)	7 (43.75)	0.261 (0.0005-0.52)	0.50	
	More nodular	11 (28.2)	28 (71.8)			
40-49	Less nodular	32 (61.5)	20 (38.5)	0.246 (0.098-0.39)	< 0.001	
	More nodular	39 (34.5)	74 (65.5)			
≥50	Less nodular	51 (78.5)	14 (21.5)	0.045 (-0.14-0.23)	0.636	
	More nodular	26 (74.3)	9 (25.7)			
Menopausal status						
Premenopausal	Less nodular	42 (62.7)	25 (37.3)	0.244 (0.117-0.37)	< 0.001	
	More nodular	54 (35.3)	99 (64.7)			
Postmenopausal	Less nodular	50 (75.8)	16 (24.2)	0.115 (0.078-0.31)	0.244	
	More nodular	22 (64.7)	12 (35.3)			
Number of parities						
0-3	Less nodular	53 (59.6)	36 (40.4)	0.199 (0.077-0.322)	< 0.001	
	More nodular	60 (38.5)	96 (61.5)			
≥4	Less nodular	39 (88.6)	5 (11.4)	0.391 (0.177-0.605)	< 0.001	
	More nodular	16 (51.6)	15 (48.4)			
Total	Less nodular	92 (69.2)	41 (30.8)	0.275 (0.17-0.38)	< 0.001	
	More nodular	76 (40.6)	111 (59.4)	. ,		

CI: Confidence interval

130

Moussavi, et al.: Mammographic density and breast nodularity

Variables	Nodular consistency	Density , <i>n</i> (%)		к (95% СІ)	Р
		Low	High		
Age (years)					
<40	Soft nodules	18 (40.0)	27 (60.0)	0.101 (-0.066-0.27)	0.234
	Hard nodules	2 (20.0)	8 (80.0)		
40-49	Soft nodules	59 (54.6)	49 (45.4)	0.291 (0.153-0.43)	< 0.001
	Hard nodules	12 (21.1)	45 (78.9)		
≥50	Soft nodules	70 (78.7)	19 (21.3)	0.102 (-0.076-0.28)	0.264
	Hard nodules	7 (63.6)	4 (36.4)		
Menopausal status					
Premenopausal	Soft nodules	80 (52.3)	73 (47.7)	0.229 (0.114-0.34)	< 0.001
	Hard nodules	16 (23.9)	51 (76.1)		
Postmenopausal	Soft nodules	67 (75.3)	22 (24.7)	0.178 (0.01-0.35)	0.038
	Hard nodules	5 (45.5)	6 (54.5)		
Number of parities					
0-3	Soft nodules	96 (54.9)	79 (45.1)	0.242 (0.133-0.35)	< 0.001
	Hard nodules	17 (24.3)	53 (75.7)		
≥4	Soft nodules	51 (76.1)	16 (23.9)	0.157 (0.038-0.35)	0.114
	Hard nodules	4 (50.0)	4 (50.0)		
Total	Soft nodules	147 (60.7)	95 (39.3)	0.256 (0.159-0.35)	< 0.001
	Hard nodules	21 (26.9)	57 (73.1)	. ,	

CI: Confidence interval

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Table 3: The relationship of mammographic density with age, menopausal status, and number of parities

Variables	Density	n (%)	Р
Age (years)			
<40	Low	20 (36.4)	< 0.001
	High	35 (63.6)	
40-49	Low	71 (43.0)	
	High	94 (57.0)	
≥50	Low	77 (77)	
	High	23 (23)	
Menopausal status			
Premenopausal	Low	96 (43.6)	< 0.001
	High	124 (56.4)	
Postmenopausal	Low	72 (72)	
	High	28 (28)	
Number of parities			
0-3	Low	113 (46.1)	< 0.001
	High	132 (53.9)	
≥4	Low	55 (73.3)	
	High	20 (26.7)	

parities. Age and gynecological history can give clues to mammographic density, in that dense breasts are predominantly seen among younger women and also those with fewer parities.^[10,13] Therefore, mammography has low sensitivity in detecting cancer among these women due to their high breast density.

This study assessed breast nodularity only through Goodson's scale. Using other scales may produce different results. Moreover, the inter- and intra-observer reliability of the scale was not assessed.

CONCLUSION

This study indicates that mammographic density has a weak agreement with breast nodularity on CBE and significant relationships with age, menopausal status, and number of parities. As Goodson's scale is a unidimensional scale, it may not be a suitable instrument to assess nodularity, and may not provide credible results to predict breast density based on nodularity. Further studies are needed to develop more comprehensive instruments for assessing not only nodule size and consistency, but also nodules distribution in all breast quadrants. Moreover, considering other factors such as age, menopausal status, and number of parities in developing a new scoring system may help to create more reliable results in predicting mammographic density.

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Conflicts of interest

There are no conflicts of interest.

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Moussavi, et al.: Mammographic density and breast nodularity

Archive of SID

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