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Comparison of Galactography, Ultrasonography and Contrast Enhanced Magnetic Resonance Imaging Findings with Pathology Results in Patients with Pathologic Nipple Discharge

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Objective: The purpose of this study was to evaluate the lesion detection rates of imaging methods by comparing galactography, ultrasonography (US) and contrast enhanced-magnetic resonance imaging (CE-MRI) findings with pathology results in patients with pathologic nipple discharge (PND).

Materials and Methods: Fifty-two female patients (age range, 18–79 years; mean age, 49,12 years) with PND were included the study. Radiologic imaging and pathology results of patients were evaluated retrospectively. The lesion detection rates of galactography, US and CE-MRI were evaluated. Galactography findings were evaluated according to modified Galactogram Image Classification System (GICS) and compared with the pathology results.

Results: Galactography was applied in 48 patients. While in 45 (93.8%) of 48 patients lesion that causes PND was found on galactography. All of the patients had breast US. In 48 (92.3%) patients, causing lesion was found on US. CE-MRI was performed in 33 of 52 patients, and lesion was found in 30 patients (90.9%). Lesion detection rates of galactography, US and CE-MRI findings were similar.

Pathology results of 48 patients (92.3%) were benign, and the results of 3 patients (5.8%) were malignant. The result of 1 patient (2%), there was no lesion on pathologic examination. The sensitivity of galactography, US and CE-MRI were 93.6%, 92.2% and 90.6%, respectively. In the double and triple combinations of imaging methods regarding the lesion detection, sensitivity was found as 100%.

There was no significant relationship between modified GICS scores and pathology results.

Conclusion: Galactography, US and CE-MRI have high sensitivity for lesion detection in patients with PND. When galactography, US and CE-MRI findings are used in double and triple combinations, lesion detection rates could be increase.

Keywords: Nipple discharge, Breast Magnetic Resonance Imaging, Galactography, Ultrasonography

1. INTRODUCTION

Nipple discharge (ND) constitutes 7-10% of all breast symptoms.[1] ND often results from benign lesions, however ND can be a symptom of breast cancers. ND occurs in malignant lesions with a rate of 2-15% in women and 20% in men.[2,3] All ND except the pregnancy and lactation are pathological. Repetitive and spontaneous discharges are usually due to benign causes. Intraductal papillomas are the most common lesions among benign causes. Spontaneous ND which is bloody and originating from single ductus should be investigated as it may be malignant, especially in patients over 50 years of age.[4,5] Causes of pathological nipple discharge (PND) can include intraductal papillomas, ductal ectasia, mastitis, fibrocystic diseases, breast cancer and Paget's disease. In patients with PND, imaging methods play an important role after clinical history and physical examination in order to determine the cause of discharge. Galactography,

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ultrasonography (US) and contrast enhanced magnetic resonance imaging (CE-MRI) are widely used radiologic methods for evaluation of PND.

In this study, we aimed to analyse the lesion detection rates of imaging methods by comparing galactography, US and CE-MRI findings with pathology results in patients presenting with PND. We also evaluated galactography findings according to the modified Galactogram Image Classification System (GICS) and compared with the pathology results.

2. MATERIALS and METHODS

This study was approved by Clinical Research Ethics Committee (Decision number: 2020/222) of our university. Informed consent was waived due to retrospective nature of the study.

281 cases admitted with PND between January 2011 and February 2020 were analyzed retrospectively. Because of the pathology results of 229 cases could not be obtained, they were excluded from the study. A total of 52 patients having pathologic diagnoses and who underwent galactography, US and CE-MRI were included in the study. All patients were female. There were maximum twenty days between imaging methods.

Galactography, US and CE-MRI examinations were evaluated by two radiologists (S.D. and E.D.) with 13 and 5 years of experience in breast imaging, in consensus, without being aware of the radiology and pathology results. The pathology results were grouped into three groups as benign, malignant and no lesion detected group.

2.1. Galactography

All galactography images were obtained in routine cranio-caudal and medio-lateral positions with Mammomat inspiration (Siemens Healthcare, Erlangen, Germany) device. In order to perform galactography, spontaneous or manipulation discharge was provided from the ductus during the examination. In galactography procedure, special galactography needles with a blunt tip of 27 gauge (G) thickness, which allow entry into the nipple, were used. For examination, standard iodized contrast agent (Omnipol, Polifarma Pharmaceuticals, İstanbul, Turkey) was injected into the ductus using 5 milliliter injectors.

The ductal system displayed on galactograms was examined for the following findings:

- Primarily, it was evaluated whether ductus is enlarged or not. Ductus diameter is less than 3 millimeter (mm) was considered normal, ductus diameter is equal or greather 3 mm was considered ductal ectasis.
- The structure of the ductus wall was evaluated whether it was smooth or irregular in shape.
- When the filling defect was observed in the ductus, the filling defect was evaluated in terms of size and single or multiple defect. While the diameter of the defect is less than 2 mm, the defect was considered as a microdefect, the diameter of defect is equal or greater than 2 mm, it was accepted as a macrodefect.[6]
- Complete or partial obstruction of the ductus and concave or suddenly ended ductus was determined.
- In the increased density areas, it was investigated whether there was a distortion of the ductus.
- It was evaluated whether erosion and irregularity in the ductus wall and there was a contrast agent penetration into the lesion.
- Finally, the location of the lesions in the ductal system (main canal, segmental canals or peripheral [subsegmental or terminal]) and their location in the breast (retroperiareolar, central, peripheral) were determined.

In galactography, the lesion that may cause PND include intraductal filling defect, ductal ectasia, irregularity or erosion of the ductus wall, was evaluated as positive. In addition, after the galactographic features were determined, a classification was made according to the Modified GICS reported by Istomin et al.[7]

2.2. US

Sonographic evaluation was performed with 6-15 MHz linear matrix array transducer (LOGIQ S7, GE Healthcare, Korea). Ultrasound examination was applied in supine position with the arm raised above the head. Axilla screening was routinely performed before or after breast screening. Cases with PND were scanned for ductal ectasis, intraductal lesions, inflammatory diseases, intensive intraductal content, lesions suspected for malignancy and fibrocystic changes. The cases with the above mentioned findings were accepted as positive.

2.3. CE-MRI

Breast CE-MRI were performed on a 1.5 Tesla MRI device (Philips Gyroscan Intera, Best, the Netherlands) with a breast coil using the routine breast CE-MRI protocol of our clinic. The patients were hospitalized in the prone position so that their breasts were placed in the coil. As a routine breast CE-MRI examination protocol, for all patients, T1 and T2 weighted turbo spin echo (TSE), Short tau inversion recovery (STIR) sequence were taken on the axial plane, precontrast and dynamic postcontrast gradient echo-3 Dimensional (3D) T1-weighted images were taken on the axial plane. According to the CE-MRI protocol, 0.1-0.2 mmol/kg contrast agent (Gadovist, Bayer Healthcare, Berlin, Germany) was used. In the dynamic study, after contrast injection, T1-weighted 3D THRIVE sequence was obtained 6 times at 80 second intervals, and the images were obtained in the axial plane. All MRI images were analysed in terms of ductal ectasis, cystic changes, inflammatory lesions, mass or non-mass type enhanced lesions. In CE-MRI imaging, imaging findings above mentioned that may cause PND were considered as positive.

2.4. Statistical analyses

SPSS 23 program was used for statistical analysis. Normality assumptions of continuous variables, Skewness and Kurtosis coefficients were investigated by Kolmogorov Smirnov test and Histogram. In the definition of categorical variables, frequency (n) and percentage (%) values are given. Independent samples t test was used to compare normally distributed continuous variables with two-level categorical variables, while one-way ANOVA was used to compare variables with three or more levels. Relationships between categorical variables were examined by Chi square analysis / Fisher's exact and Mc-Nemar tests. Finally, the sensitivity values were calculated when comparing the findings obtained with the gold standard accepted pathology results. In all analyzes, $p<0.05$ value was accepted as the level of significance.

3. RESULTS

A total of 52 patients with PND were included in the study. The age of the patients varied between 18 and 79 years, and the mean age was 49.12 years. The mean age of the 3 patients who were malignant as a result of pathology was 54 years, and the mean age of 48 patients who were benign was 48.1.

Galactography was not applied in 4 patients (7.7%) due to the absence of discharge on the day of the examination. While in 45 (93.8%) of 48 patients who had galactography, lesion that causes ND was found, in 3 patients (6.3%), no lesion was detected.

Breast US was made in all of the patients. In 48 (92.3%) patients, lesion that causes ND was found, however in 4 patients (7.7%) any lesion was not detected.

CE-MRI was performed in 33 of 52 patients, and lesion that causes ND was found in 30 patients (90.9%), in 3 patients (9.1%) no lesion was detected (Figure 1).

Pathology results of the patients were presented in table 1. Pathology results accepted as gold standard for final diagnosis. Pathology results of 48 patients (92.3%) were benign, and the results of 3 patients (5.8%) were malignant causes. The result of 1 patient (2%), there was no lesion on pathologic examination.

According to modified GICS based on galactography images; 3 patients (6.25%) were classified as GICS 1, 5 patients (10.4%) were classified as GICS 2, 22 patients (45.8%) were classified as GICS 4A, 15 patients (31.25%) were classified as GICS 4B, 2 patients (4.1%) were classified as GICS 4C, And finally 1 patient (2.08%) was classified as GICS 5.

In 48 patients who have both galactography and US examination, it was investigated whether there was a significant difference between galactography and US examination to detect the lesion that may cause ND. In 45 of the 48 patients, galactography was positive for lesion detection. In 41 (91.1%) of these 45 patients, lesions were detected with both galactography and US (Figure 2). In 3 cases with negative galactography finding, caused lesion was detected on US. In 2 of these 3 patients, ductal ectasia and intraductal papilloma were seen on US, and the other patient had BI-RADS 4 lesion on US. It was found that there was no statistically significant difference between the two examinations in terms of lesion detection (p= 1.00).

In 31 patients who have both CE-MRI and galactography examinations, the difference between galactography and CE-MRI in terms of lesion detection was analyzed. In 26 (89.7%) of 29 patients who had lesion on galactography, the lesions were also detected on CE-MRI. In two patients, lesions were detected with CE-MRI, whereas lesions could not be detected on galactography. In the analysis, there was no statistically significant difference between the two examinations in terms of lesion detection (p= 1.00).

In 33 patients who have both US and CE-MRI examinations, it was investigated whether there was a significant difference between US and CE-MRI in terms of determining the lesion that may cause ND. 27 (90%) of the 30 patients who had lesion on US, lesions were also detected on CE-MRI. In 3 patients lesions were detected with CE-MRI, whereas no lesions were detected on US. It was found that there was no statistically significant difference between lesions detection rate of two tests (p= 1.00).

The sensitivity of galactography for lesion detection was 93.6% when pathology results were accepted as gold standart. Pathology results of 3 patients who have no lesion on galactography were intraductal papillomatosis and intraductal papilloma.

When US results were compared with the pathology results, sensitivity of US for lesion detection was found 92.2%. Pathology results of 4 patients where there is no lesion on US were reported as simple intraductal hyperplasia, fibrocystic changes, intraductal papilloma and intraductal papillomatosis.

The sensitivity of CE-MRI for lesion detection was found 90.6%. Pathology results of 3 patients where there is no lesion detected on CE-MRI were reported as intraductal papilloma and atypical intraductal papillomatosis.

In 31 patients who have galactography, US and CE-MRI examinations, sensitivity was determined as follows; Cases in which a lesion was detected

in any of the three examinations were classified as positive, and cases in which no lesion was detected in all three examinations were classified as negative. Sensitivity value was 100% for lesion detection in patients who have triple radiologic examinations.

In 33 patients who have both US and CE-MRI examinations, sensitivity value was 100% for lesion detection.

In 48 patients who have both galactography and US examinations, sensitivity value was 100% for lesion detection.

In 31 patients who have both galactography and CE-MRI examinations, sensitivity value was 100% for lesion detection.

It was investigated whether there is a significant relationship between pathology results and Modified GICS score in patients who have galactography examination. These results were showed in table 2. In the analysis, it was found that there was no significant relationship between modified GICS scores and pathology results (p= 0.377).

Table 1.

Pathology results of patients

Pathologic Diagnosis	**Patients (n)**
Benign	
Ductal ectasis	15
Ductal ectasis and intraductal papilloma	1
Ductal ectasis and fibrocystic changes	1
Ductal adenoma	2
Fibrocystic changes	3
Fibrocystic changes and intraductal papilloma	2
Intraductal papillomatosis and fibrocystic changes	1
Fibrocystic changes and fat necrosis	2
Intraductal papilloma	10
Intraductal papillomatosis	2
Atypical intraductal papilloma	3
Atypic intraductal papillomatosis	2
Granulomatous mastitis	1
Malignant	
Invasive papillary carcinoma	1
Ductal carcinoma in situ	2
No lesion	1

Table 2.

Comparing the Modified GICS scores and pathology results of patients

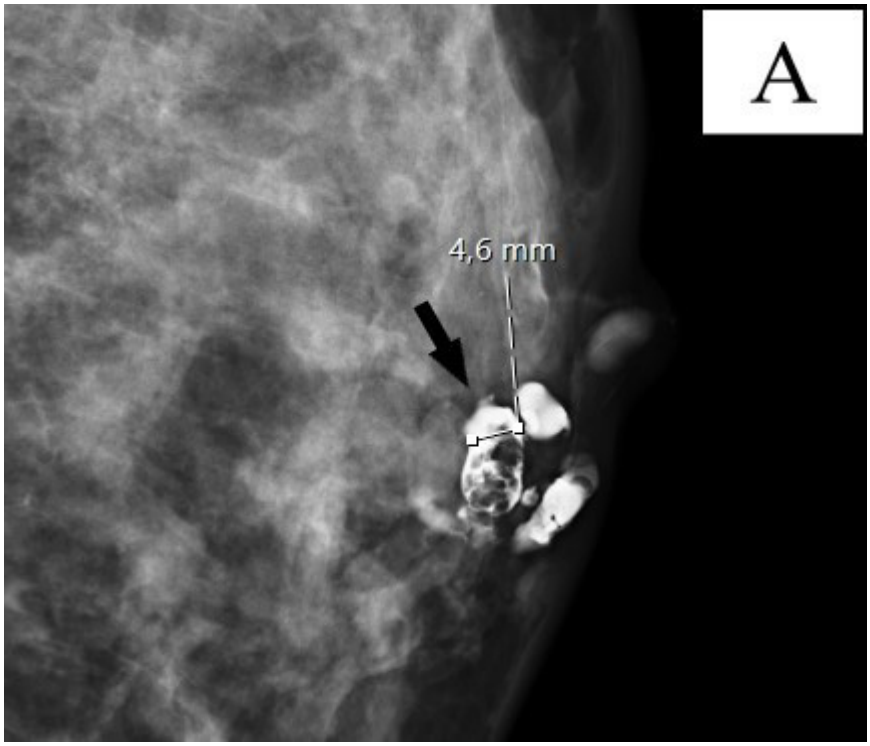
	Pathology results			
	Benign n (%)	Malignant n (%)	No lesion	p value
Modified GICS score				0.377
GICS 1	2 (4.5)	1 (33.3)	0 (0)	
GICS 2	5 (11.3)	0 (0)	0 (0)	
GICS 4A	21 (47.7)	1 (33.3)	0 (0)	
GICS 4B	14 (31.8)	0 (0)	1 (100)	
GICS 4C	2 (4.5)	0 (0)	0 (0)	
GICS 5	0 (0)	1 (33.3)	0 (0)	

GICS: Galactogram Image Classification System

Figure legends

Figure 1.

38-year-old woman with pathologic nipple discharge. Galactography (A) shows dilated ductus and intraductal filling defect (black arrow) in left breast. Contrast enhanced lesion (white arrow) is seen on CE-MRI (B) compatible with filling defect on galactography. Pathologic result of this lesion is intraductal papilloma and severe intraductal hyperplasia.



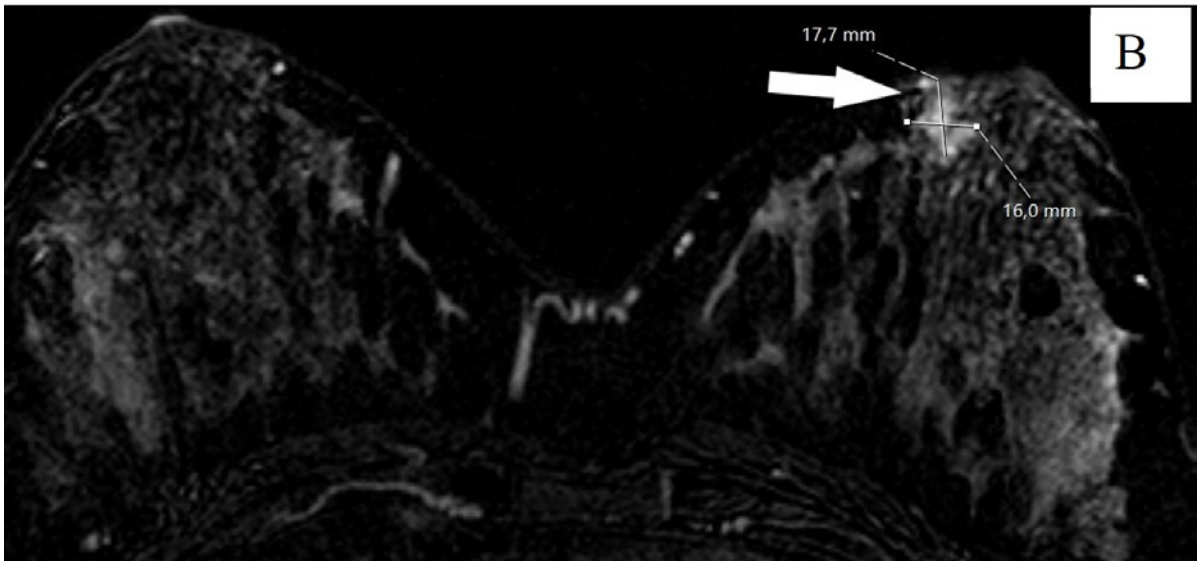
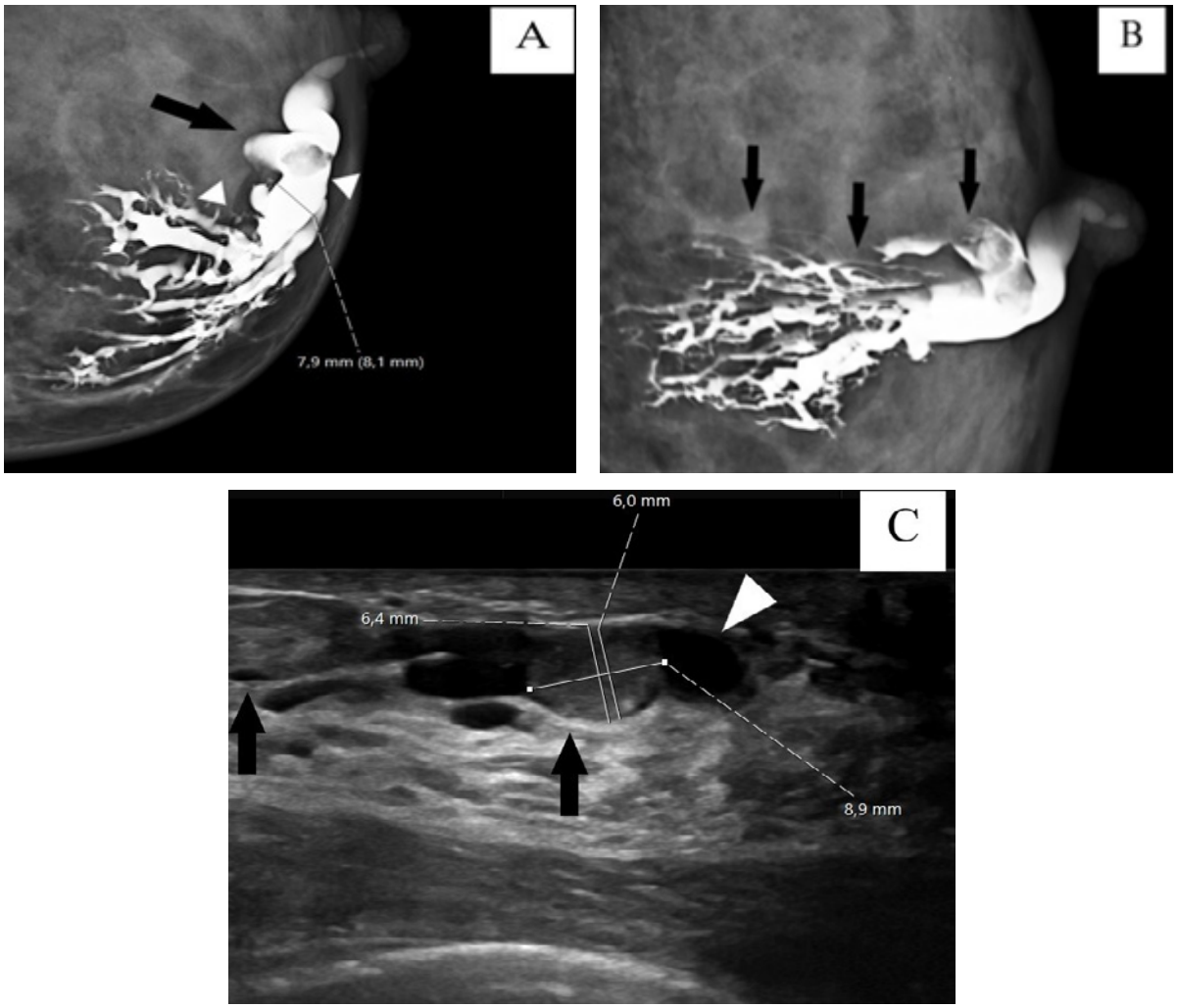


Figure 2.

31-year-old woman with pathologic nipple discharge. Galactography images (A,B) shows multiple dilated ductuses and multiple filling defects in left breast. Ultrasonography image (C) shows dilated ductuses (white arrowhead) and multiple intraductal solid lesions (black arrows). Pathologic result of these lesions is intraductal papillomatosis.



4. DISCUSSION

In this study, the lesion detection rates of imaging methods in patients with PND were evaluated by comparing with pathologic results. The sensitivity of galactography, US and CE-MRI for lesion detection were 93.6%, 92.2%, and 90.6%, respectively. There was no statistically significant difference between lesions detection rate of two tests in patients with double radiological examinations. When galactography, US and CE-MRI findings are used in double and triple combinations, lesion detection rates were increase. Sensitivity value was 100% for lesion detection in patients who have double and triple radiologic examinations.

ND that is seen at an older age is mostly caused by malignancy.[8] Berna-Serna et al. reported that solitary intraductal papilloma and intraductal papillomatosis were generally found in young women (<50 years).[6] In their study, the result of pathology was reported as carcinoma in 3 patients aged 50 years. In this study, there are 3 patients with pathological malignancy and the average age is 54. The average age of 48 patients whose pathology was benign was calculated as 48.1. The findings are consistent with the literature.

According to the our pathology results, ND was observed to occur more frequently due to benign lesions and this situation was found to be compatible with the literature. In the study reported by Zaky et al., benign lesions (74.2%) were more likely to cause PND.[9] The high risk lesion and malignancy rate was determined as 25.8%. In a study by Paula et al. the most common causes were benign lesions such as ductal ectasis in 6-59% and papilloma in 35-56%.[10] They stated that the underlying malignancy risk ranged from 5 to 23%. In this study, the pathology results of 48 patients (92.3%) were benign causes, and the results of 3 patients (5.8%) were malignant causes.

In the study of Jung et al., it was stated that galactography was superior than US to detect intraductal lesion.[11] In the study of Chung et al. the US could detect all 15 lesions (8 papillary and 7 malignancies), while galactography could not detect 3 of 15 lesions.[12] They thought that US was superior to detect lesions. Hild et al. compared US and galactography in 35 cases to detect any ductus-related pathology.[13] While US findings were positive in 26 cases (74%), galactographic findings were found positive in 19 (54%) cases. In this study, lesions were detected on US examination in 41 (91.1%) of 45 cases in whom lesions were detected on galactography. In 3 cases in which no lesion was detected on galactography, caused lesion was detected in US. There was no statistically difference between the two imaging methods in terms of lesion detection.

In a study by Hirose et al., it was stated that CE-MRI is superior than galactography to detect lesions.[14] Manganaro et al. investigated the difference between galactography and CE-MRI examinations to detect benign and malignant lesions.[15] It has been stated that CE-MRI is superior than galactography in terms of both detection and classification lesions as benign or malignant. In this study, lesions of 26 of 29 patients in whom lesions were detected on galactography were also detected on CE-MRI. In 2 patients whose lesion was not detected on galactography, causative lesion was detected on MRI. No statistically significant difference was detected between the two imaging methods in terms of lesion detection.

In a study by Yılmaz et al., it is stated that CE-MRI is superior than US to detect lesions that cause ND.[16] In this study, lesions were detected on CE-MRI in 27 (90%) of 30 cases with lesions detected on US. Lesions were detected on CE-MRI in 3 patients whose lesion was not detected on US. The results of US and CE-MRI methods were statistically similar.

Ohlinger et al. evaluated the relationship between the detection of any lesions that may cause ND on galactography and the detection of benign or malignant lesions as a result of pathology, and the sensitivity of the galactography was indicated as 81% and specificity as 44,4%.[17] In a few other studies in the literature, it was stated that sensitivity varies between 50-94%, while specificity varies between 41-64%.[18-21] In this study, the sensitivity was 93% and compatible with the literature.

There are different values in the literature regarding to lesion detection of US. In the study conducted by Ohlinger et al., sensitivity and specificity of US in terms of lesion detection were 82.9% and 17.9%.[17] In the study of Grunwald et al., sensitivity was 67.3% and specificity was 61.5%.[22] In the study of Adepoju et al., sensitivity and specificity were reported as 36% and 68%, respectively.[23] In the study of Vargas et al., sensitivity and specificity were stated as 26% and 97%, respectively.[19] In this study, the sensitivity was determined as 92.2%, this value was higher than reported sensitivity values.

Ohlinger et al. reported that sensitivity and specificity of CE-MRI were has a lesion 82.5% and 11.8%, respectively in terms of lesion detection.[17] Nakahara et al. and Ishikawa et al. reported that sensitivity and specificity were 75%.[24,25] Liberman et al. stated in their study that sensitivity was 86-100% and specificity was 39-97%.[26] In this study, sensitivity was determined as 90.6%. Sensitivity of the study was compatible with the literature.

According to our knowledge, no study has been found in the literature that galactography, US and CE-MRI were used together for lesion detection. In the study of Blum et al., when US and galactography were used together, the sensitivity was 91% and the specificity was 17%.[27] In this study, when three imaging methods used together, the sensitivity was calculated 100%. The use of different evaluation criteria on galactography, US, and CE-MRI increases the sensitivity. While galactography shows changes in the duct, it can also detect microcalcifications and differences in breast density. The disadvantage of galactography is that it sometimes cannot determine clearly whether the lesion is inside or outside of the duct. Galactography has been evaluated as useful for determining irregularities and possible fibrotic changes in the ductus wall. US allows evaluation of both breast parenchyma and dilated ductal structures. CE-MRI has capability of show both morphologic evaluation and contrast enhancement features of breast tissue and lesions

Galactography imaging findings such as ductal stenosis, ductus wall irregularity, sudden ductal interruption, periductal contrast extravasation, sacculation, intraductal irregular shaped filling defects, and ductal distortion may suggestive for malignancy.[6,28-30]. Berna-Serna et al. reported that the pathology results of patients classified as GICS 5 were compatible with carcinoma and galactography may be useful in distinguishing benign-malignant lesions.[6] In the same study, most of GICS 3 lesions were intraductal papilloma, and GICS 4 lesions were papillomatosis. Istomin et al. reported that the pathology results of some patients in GICS 4B and 5 categories were benign, and DCIS was detected in a patient classified as GICS 1.[7] In our study, 3 patients reported as malignant were classified in GICS 1, GICS 4A, and GICS 5 categories. The diagnostic accuracy of modified GICS could not be fully evaluated because number of malignant lesions (n=3) was small.

There were some limitations in this study. Firstly, the study was a retrospective study and the study's power was reduced due to small sample size. Secondly, the specificity assessments of galactography, US, and CE-MRI individually and combinations of them could not be calculated due

to the absence of lesions in 1 patient on pathology while imaging methods show lesion. The other limitations was that interobserver variability was not studied.

5. CONCLUSION

Galactography, US and CE-MRI have high sensitivity for lesion detection in patients with PND. When galactography, US and CE-MRI findings are used in double and triple combinations, lesion detection rates could be increase.

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Conflict of Interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This single institutional study was approved by Clinical Research Ethics Committee (Decision number: 2020/222) of our university.

REFERENCES

1. Pena KS, Rosenfeld JA. Evaluation and treatment of galactorrhea. Am. Fam. Physician 2001;63:1763-70.
2. Hussain AN, Policarpio C, Vincent MT. Evaluating nipple discharge. Obstet Gynecol Surv. 2006;61:278-83.
3. Sakorafas GH. Nipple discharge: current diagnostic and therapeutic approaches. Cancer Treat Rev. 2001;27:275-82.
4. Becker S, Choti M: Breast diseases. In: The Johns Hopkins Manual of Gynecology and Obstetrics. Bankowski, BJ, Hearne, AE, Lambrou, NC, Fox, HE, Wallach, EE (Eds). Lippincott, Williams & Wilkins, PA, USA (2002).
5. Simmons R, Adamovich T, Brennan M, Christos P, Schultz M, Eisen C, et al. Nonsurgical evaluation of pathologic nipple discharge. Ann. Surg. Oncol. 2003;10:113-6.
6. Berna-Serna JD, Torres-Ales C, Berna-Mestre JD, Sola-Perez J, Canteras-Jordana M. Galactography: An application of the galactogram imaging classification system (GICS). Acta Radiol 2010;51(2):128-36.
7. Istomin A, Masarwah A, Pitka¨nen M, Joukainen S, Sutela A, Vanninen R, et al. Galactography is not an obsolete investigation inthe evaluation of pathological nipple discharge. PLoS ONE 2018;13(10):e0204326.
8. Lau S, Chenmeister IK, Stachs A, Gerber B, Krause A, Reimer T. Pathologic nipple discharge: surgery is imperative in postmenopausal women. Ann Surg Oncol 2005;12:246-51.
9. Zaky M.M, Hafez A, Zaky M.M, Shoma A, Soliman N, Elmokadem A.H. MRI For Assessment Of Pathologic Nipple Discharge: İs İt Mandatory? Egypt J Radiol Nucl Med. 2019;50:92.
10. Paula IB, Campos AM. Breast imaging in patients with nipple discharge. Radiol Bras 2017; 50(6):383-8
11. Jung Hk, Park Ym, Baek Hj, Choo Hj, Kim Ek, Kim Dw, et al. Comparison Between Ultrasonography And Galactography İn Detecting Lesions In Patients With Pathologic Nipple Discharge. Ultrasound Q. 2019;35(1):93-8.
12. Chung SY, Lee KW, Park KS, Lee Y, Bae SH. Breast tumors associated with nipple discharge: correlation of findings on galactography and sonography. Clin Imaging 1995;19:165-71.
13. Hild F, Duda VF, Schulz KD. Ductal orientated sonography improves the diagnosis of pathological nipple discharge of the female breast compared with galactography. Eur J Cancer Prev 1998;7(suppl 1):S57-62.
14. Hirose M, Nabusawa H, Gokan T. MR ductography: comparison with conventional ductography as a diagnostic method in patients with nipple discharge. Radiographics 2007;27(suppl 1):S183-96.
15. Manganaro L, D'Ambrosio I, Gigli S, Di Pastena F, Giraldi G, Tardioli S, et al. Breast MRI in patients with unilateral bloody and serous-bloody nipple discharge: a comparison with galactography. Biomed Res Int. 2015:806368.
16. Yılmaz R, Bender O,Yabul F.Ç, Dursun M, Tunacı M, Acunas G. Diagnosis of Nipple Discharge: Value of Magnetic Resonance Imaging and Ultrasonography in Comparison with Ductoscopy Balkan Med J. 2017;34(2):119-26.
17. Ohlinger R, Stomps A, Paepke S, Blohmer JU, Grunwald S, Hahndorf W, et al. Ductoscopic detection of intraductal lesions in cases of pathologic nipple discharge in comparison with standard diagnostics: the German multicenter study. Oncol Res Treat. 2014;37(11):628-32.
18. Adepoju LJ, Chun J, El-Tamer M, Ditkoff BA, Schnabel F, Joseph KA. The value of clinical characteristics and breast-imaging studies in predicting a histopathologic diagnosis of cancer or high-risk lesion in patients with spontaneous nipple discharge. Am J Surg 2005;190:644-6.
19. Vargas HI, Vargas MP, Eldrageely K, Gonzalez KD, Khalkhali I. Outcomes of clinical and surgical assessment of women with pathological nipple discharge. Am Surg 2006;72:124-8.
20. Hahn M, Krainick-Strobel U, Toellner T, Gissler J, Kluge

S, Krapfl E, et al. Minimally Invasive Breast Intervention Study Group (AG MiMi) of the German Society of Senology (DGS); Study Group for Breast Ultrasonography of the German Society for Ultrasound in Medicine (DEGUM) Interdisciplinary consensus recommendations for the use of vacuum-assisted breast biopsy under sonographic guidance: first update 2012. Ultraschall Med 2012;33:366-71.

21. Morrog M, Morris EA, Libermann L, Borgen PI, King TA. The predictive values of ductography and magnetic resonance imaging in the management of nipple discharge. Ann Surg Oncol 2007;12:3369-77.
22. Grunwald S, Heyer H, Paepke S, Schwesinger G, Schimming A, Hahn M,et al. Diagnostic value of ductoscopy in the diagnosis of nipple discharge and intraductal proliferations in comparison to Standard methods. Onkologie 2007;30:243-8.
23. Albrecht C, Thele F, Grunwald S, Kohlmann T, Hegenscheid K, Utpatel K. et al. Nipple discharge: role of ductoscopy in comparison with standard diagnostic tests. Onkologie 2013;36:12-6.
24. Nakahara H, Namba K, Watanaba R, Furusawa H, Matsu T, Akiyama F, et al. A comparison of MR imaging, galactography and ultrasonography in patients with nipple discharge. Breast Cancer 2003;10:320-9.
25. Ishikawa T, Momiyama N, Hamaguchi Y, Takeuchi M, Iwasawa T, Yoshida T, et al. Evaluation of Dynamics studies of MR mammography for the diagnosis of intraductal lesions with nipple discharge. Breast Cancer 2004;11:288-94.
26. Liberman L, Morris EA, Dershaw DD, Abramson AF, Tan LK. Ductal enhancement on MR imaging of the breast. Am J Roentgenol 2003;181:519-25.
27. Blum KS, Rubbert C, Antoch G, Mohrmann S, Obenauer S. Diagnostic accuracy of abnormal galactographic and sonographic findings in the diagnosis of intraductal pathology in patients with abnormal nipple discharge. Clin Imaging. 2015;39(4):587-91.
28. Dinkel HP, Trusen A, Gassel AM, Rominger M, Lourens S, Müller T, et al. Predictive value of galactographic patterns for benign and malignant neoplasms of the breast in patients with nipple discharge. Br J Radiol 2000;73:706-14.
29. Hou MF, Huang TJ, Liu GC. The diagnostic value of galactography in patients with nipple discharge. Clin Imaging 2001;25:75-81.
30. Kim SH, Cha ES, Kim HS, Kang BJ, Choi JJ, Jung JH. Galactography acquired with digital mammography in patients with nipple discharge: a retrospective analysis. Arch Gynecol Obstet 2009;280:217-22.