ONCOLOGÍA
roe-solca.ec
ORIGINAL ARTICLE

The usefulness of mammography and ultrasound in dense fibroglandular tissue for breast cancer screening

Rodrigo Fabian Díaz Pérez [1], **Johana A. Arriciaga Vázquez** [1]

1. Imaging Specialty, Postgraduate Coordination, Faculty of Medical Sciences, University of Guayaquil, Ecuador

***Correspondence:**
el.rodris@hotmail.com

Address:
Av. Delta, Guayaquil 090510 -Ecuador. Phone: (593) 04 228-4505.

Conflict of interest: Los autores declaran no tener conflictos de intereses.

Received: September 28, 2022
Accepted: October 24, 2022
Published: December 7, 2022
Editor: Dra. Evelyn Valencia Espinoza.

Cite:
Díaz R, Arriciaga J. The usefulness of mammography and ultrasound in dense fibroglandular tissue for breast cancer screening. Rev. Oncol. Ecu 2022;32(3):310-319.

ISSN: 2661-6653

DOI: https://doi.org/10.33821/664

Summary

Introduction: Mammography is the method of choice for diagnosing breast cancer; however, its performance in breasts with dense tissues decreases. The present study aimed to establish the value of mammography and ultrasound for breast cancer screening in women with dense glandular tissues.

Methodology: A cross-sectional study was carried out, which included, for convenience, 97 consecutive cases of women with dense glandular tissue on mammography, to which a complementary ultrasound study was performed, attended between 01-01-2017 and 12-31-2019 in the Imaging service. Teodoro Maldonado Carbo Hospital. Those who had a study of breast lesions by biopsy and pathology were included. For method analysis, sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, and the percentage of tests correctly performed were calculated.

Results: The prevalence of breast cancer in the sample was 95%. For the mammographic BI-RADS, the diagnostic yield was DC 12.37%, S 7.61%, E 98.13%, PPV 98.68%, NPV 5.56%, CPP NV, and CPN 0.92. For the ultrasound BI-RADS, it was DC 43.30%, S 41.30%, E 80%, PPV 97.44, NPV 6.90%, CPP 2.07, and CPN 0.73. The sonographer's criteria were DC 86.60%, S 91.30%, E 8.00%, PPV 94.38, NPV 5.56%, CPP 0.91, and CPN NV.

Conclusion: Mammography had poor performance. In ultrasound, the use of BIRADS improves performance. The criterion issued by an experienced sonographer achieves the best performance for diagnosing breast malignancy in women with dense fibroglandular tissue.

Keywords:
MESH: Breast Neoplasms, Ultrasonography, Mammography, Diagnostic Services

Introduction

Breast cancer is the leading cause of death for women worldwide [1]. Adequate access to breast cancer imaging screening is the first step on the diagnostic pathway to decrease mortality from this disease. Early diagnosis is essential for treatment and prognosis, as patients with smaller primary cancers at diagnosis have a significantly higher survival rate and a lower chance of dying from cancer [2]. Early detection of breast cancer and accurate assessment of

lesions have become the goals of several imaging modalities, which are currently the most valuable tools for breast cancer screening.

Mammography has long been considered the gold standard for screening and early detection of breast cancer; however, this is not always the case, as it is imperfect, particularly for women with dense breasts. Breast density refers to the relative amounts of fat and glandular tissue in the breast. The range in density from nearly all fat to nearly all glandular tissue affects the mammographic appearance of the breast [3]. Mammography is a diagnostic imaging modality that uses ionizing radiation, and in screening studies, a mediolateral oblique and craniocaudal projection of each breast are obtained. Consequently, dense breasts, having a more significant amount of cellular components, both epithelial and stromal, attenuate X-rays in a more significant proportion concerning fatty breasts, which are radiolucent, which makes imaging assessment difficult, since a dimming effect is produced masking lesions that may be malignant but may also signify an independent risk factor for cancer [4]. Instead, breast ultrasonography is an exceptionally effective tool for palpable imaging abnormalities in the breast. It distinguishes cystic masses from solid masses and demonstrates the characteristics of solid lesions that denote it as suspicious and a candidate for justified biopsy. If a biopsy is needed, ultrasound is the ideal imaging tool to guide subsequent procedures, further enhancing its usefulness in diagnosing breast cancer. This diagnostic method is a modality that can be useful in dense breast tissue because it is in the ability to detect breast cancer that mammography reports dense glandular tissue as it is an echorefringent structure; however, the sensitivity and specificity of the method is highly variable in different studies [5]. Ultrasound is a technique that is based on the processing of ultrasound, emitted by a transducer toward a region of the body that we wish to study. In the case of the mammary gland, the use of high-frequency linear probes results in a highly defined image, allowing the observation of tissues whose histological composition results in a diagnostic limitation when examined with other methods such as mammography, also because it has other technological applications, such as the use of color Doppler that provides additional information on a suspicious lesion, and because it does not use ionizing radiation [6].

Approximately 20% of breast cancers are not detected due to dense glandular tissue in the breast at the time of the mammography examination. On the other hand, women with extremely dense breasts have a 4.7 times higher risk of developing breast cancer, but mammography is less effective. Cancers detected in women with dense breasts are more significant and more frequently node-positive. Interval cancers, which have a worse prognosis than screen-detected cancers, are 18 times more likely to occur in women with dense breasts. This is even more significant when it considers that more than half of American women have dense breast tissue. Given the prevalence of dense breast tissue and the challenges of identifying cancer in dense breasts with mammography, additional imaging modalities are needed to detect mammographically occult breast cancer [3].

The present study aimed to perform a diagnostic test of mammography compared with breast ultrasound in women with dense glandular tissues.

Materials and methods

Study design

The present study is observational. The source is prospective.

Study area

The study was carried out in the imaging service of the Teodoro Maldonado Carbo Specialty Hospital of the Ecuadorian Institute of Social Security in Guayaquil-Ecuador. The study period was from January 1, 2017, to December 31, 2019.

Universe and scenery

The universe was made up of all the patients registered in the institution. The sample size calculation was nonprobabilistic, census type, where all incident cases in the study period were included.

Participants

Cases of patients with dense glandular tissue in whom mammography and ultrasound were requested and underwent biopsy or surgical excision of the breast lesion were included; additionally, in patients, there was a definitive diagnosis by histopathology. Pregnant women with a previous history of breast cancer were excluded.

Variables

The descriptive variables were age, menopause, family history of breast cancer, clinical manifestations, histopathological diagnosis, mammographic diagnosis, and ultrasound diagnosis.

Procedures, techniques, and instruments.

The data were collected directly from the patient prior to the patient's signature of authorization; other complementary data later, such as the histopathological diagnosis, were taken from the institutional electronic file (AS400) in a form designed exclusively for this purpose.

Avoidance of bias

To guarantee the reliability of the information, the researchers were trained in data collection and the use of the AS400 system. A double checklist was used to include the cases, and the principal investigator validated and cured the data. The institution's on-duty medical specialists performed ultrasounds and mammograms.

Statistical analysis

Once the information was compiled in an Excel spreadsheet, it was entered into a data matrix of SPSS™ 25.0 software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Descriptive statistics were used based on frequencies and percentages for the qualitative variables and the quantitative measures of central tendency. A diagnostic test is performed with the standard histopathology method, comparing the results of mammograms and ultrasounds.

Results

The analysis included 97 patients.

Clinical characterization

The age group with the highest observations among the women studied was 50 to 59, and 73.2% were 50 years or older. The mean age for the study group was 59 ± 12 years, with the lowest reported age being 36 years and the maximum being 85 years.

Regarding a pathological family history related to breast cancer, 89.7% did not have it, and 10.3% did. Most of these antecedents were breast cancer; the second reported was colon cancer. A total of 71.1% had a history of already being in the menopause period. A total of 69.1% of the patients studied had already been pregnant, and 22.7% had used contraceptives. The use of hormone replacement therapy was only reported by 5.2% of the women studied. A history of previous breast lesions was only reported by 13.4% of the patients (Table 1).

Table 1. Distribution of the sample according to demographic characteristics and personal history.

Characteristic		Frequency	Percentage
Age Classification	30 – 39 years	two	2.1
	40 – 49 years	22	22.7
	50 – 59 years	30	30.9
	60 – 69 years	23	23.7
	70 – 79 years	14	14.4
	80 – 89 years	6	6.2
Family Pathological History	Colon cancer	two	2.1
	breast cancer	8	8.2
	None	87	89.7
Menopause		69	71.1
Previous pregnancies		67	69.1
Use of contraceptives		22	22.7
Use of hormone replacement therapy		5	5.2
History of previous breast injury		13	13.4

Among the imaging characteristics of the breast, 85.6% were classified with an American College of Radiology (ACR) score of 3 (Table 2). The classification of breast lesions by BI-RADS using mammography showed that 78.4% were classified with a score of 0, followed by 7.2% for a score of 2 and with a similar value for a score of 5 (Table 2). The classification of breast lesions by BIRADS using ultrasound showed that 55.7% were classified with a score of 4, followed by 39.2% with a score of 5 (Table 2).

Table 1. Characteristics in patients with dense breast tissue under study for suspected breast cancer.

Characteristic		Frequency (n=97)	Percentage
ACR Classification	3	83	85.6
	4	14	14.4
Mammographic BIRADS	0	76	78.4
	2	7	7.2
	5	7	7.2
	4	5	5.2
	3	1	1.0
	4A	1	1.0
BIRADS Ultrasound	4	54	55.7
	5	38	39.2
	2	3	3.1
	3	1	1.0
	6	1	1.0
Diagnosis of the high probability of malignancy by ultrasound		89	91.8

The most frequent diagnosis among the neoplasms was invasive ductal carcinoma, which represented 80.4% of the cases, followed in frequency by invasive lobular, papillary, and ductal carcinomas in situ with 2% of all of them. Two nonmalignant lesions were reported as the most frequent, fibroadenoma and fibrofatty tissue, with 2.1% each. Other malignant neoplasm lesions were reported less frequently (Table 3).

Table3. Histopathological diagnosis of breast lesions.

Diagnosis	Frequency (n=97)	Percentage
Invasive Ductal Carcinoma	77	80.4
Invasive Lobular Carcinoma	2	2.1
papillary carcinoma	2	2.1
Ductal carcinoma in situ	2	2.1
fibroadenoma	2	2.1
fibrofatty tissue	2	2.1
Invasive Mucinous Adenocarcinoma	1	0.9
Invasive Papillary Adenocarcinoma	1	0.9
Invasive Ductal Carcinoma Mucinous Type	1	0.9
Invasive Ductal Carcinoma With Desmoplasia.	1	0.9
Invasive Mixed Ductal-Lobular Carcinoma	1	0.9
Mucinous carcinoma in situ	1	0.9
Non-Hodgkin's Lymphoma	1	0.9
Metastasis of Ductal Carcinoma of the Breast	1	0.9
Phyllodes tumor	1	0.9

Diagnostic tests

When the BI-RADS classification was used to classify mammographic lesions classified as highly suspicious for malignancy (n=7), 100% resulted in a diagnosis of malignancy, while no lesions were detected with this classification. A histopathological study reported that it was benign. When BIRADS indicated no suspicion of a high risk of malignancy (n= 90), 94.4% were diagnosed as malignant neoplasms, and 5.6% were reported as benign (Table 4).

Table 4. Diagnostic tests.

	Malignant neoplasm by histopathological study yes=92	no=5	Sensitivity	specificity	PPV	VPN	Correct dx
BIRADS by mammography (Positive)	7 (7.6%)	0 (0%)	7.61% (3.4-15.6%)	98.13% (46.3-100%)	98.68% (56.1-100%)	5.56% (2.1-13.1%)	12.4% (6.8-21.0%)
BIRADS by ultrasound (Positive)	38 (41.3%)	1 (20%)	41.3% (31.3-52.1%)	80.0 (29.9-99.0%)	97.4% (84.9-99.9%)	6.9% (2.2-17.6%)	43.3 (33.4%-53.7%)

PPV: positive predictive value. NPV: negative predictive value. DX: Diagnosis

The diagnostic performance of the use of the BIRADS classification in mammography to detect malignant neoplastic lesions made it possible to demonstrate a correct diagnosis in 12.37% of the cases; table 4 shows the confidence interval for a proportion. The relationship between the percentage of true positives and the percentage of false positives could not be assessed, while the percentage of false negatives and the percentage of true negatives was 0.92 (range 0.87 - 0.98). The diagnostic performance of the use of the BIRADS classification in ultrasound to detect malignant neoplastic lesions made it possible to demonstrate a correct diagnosis in 43.30% of the cases (range 33.40% - 53.74%). The percentage of true positives between the percentage of false positives was 2.07 (0.35 - 12.12), while the percentage of false negatives between the percentage of true negatives was 0.73 (range 0.46 - 1.17) (Table 4).

Discussion

Under normal breast density conditions, mammography and breast ultrasound have outstanding diagnostic performance [7], with sensitivity and specificity performances of 73% and 80%, respectively. In the present study, a notable drop in diagnostic performance can be observed in mammography when dealing with dense tissue with an ACR of 3-4.

In the present study, the low performance of mammography in this type of tissue is observed, as well as the application of the BIRADS geographic criteria. This finding is in contrast to what was reported by Luo and colleagues (2019) [8], who instead found that a normalization that incorporates the BI-RADS category produces better discrimination (P =0.011). In contrast, ultrasound performed by an experienced operator may change the perspective and increase the effectiveness of the examination, as indeed occurred with increased detection of breast cancers by ultrasound, although sensitivity yielded poor results. It has been reported that a program of continuous breast cancer screening using ultrasound in women with dense breast tissue can detect otherwise occult malignancies with a low biopsy rate [9].

What happened in the study may be because breast density in the case of mammography would prevent the BIRADS criteria from having a greater weight in the diagnostic decision of the specialist who interprets the images, although the fact of experience may override this and for the operator to incorporate other parameters into his imaging evaluation. In this regard, a study [10] reported that the sensitivity of mammography for breast cancer diagnosis was high,

approximately 80%, in women with a BIRADS density score of 1 and MTR markers of 1 or 2. The sensitivity was low, 67%, in women with BIRADS density score two and MTR marker 4. For women with BIRADS density scores of 3 and 4, the already low sensitivity was further reduced for women with MTR marker 4.

The performance of ultrasound draws attention. However, the decrease in specificity may be due to 2 fundamental facts: first, the population with dense breast tissue has a higher risk of having malignant lesions than those with breasts with an average density of fibroglandular breast tissue, as has been mentioned by several authors. [11, 12]. Second, the request was made in patients who had been indicated for a mammography study to rule out breast cancer since the Teodoro Maldonado Hospital is a third-level institution; therefore, the prevalence of malignant lesions was high, with a low rate of benign lesions, which could interfere with the result.

Conclusions

Mammography performs poorly in assessing malignant neoplastic lesions in the breast when applied to women with dense breast tissue, despite using BIRADS criteria. Although the use of the BIRADS classification has become an imponderable aid in imaging practice, it is no less accurate that experience plays a fundamental role in the imaging study of the breast with a breast lesion, and this is evident when it was observed that most of the diagnoses correctly made with malignant lesions occurred when the sonographer issued his diagnostic criteria.

Acknowledgments

The authors thank the employees and patients of the Hospital de Especialidades Teodoro Maldonado Carbo of the Ecuadorian Institute of Social Security, who collaborated in developing this research.

Administrative information

Abbreviations

BI-RADS: Breast Imaging Reporting and Data System.
PPV: positive predictive value.
NPV: negative predictive value.
DX: diagnosis.

Additional Files

None declared by the authors.

Financing

The authors did not receive any financial recognition for this research work. The expenses incurred in this study constitute the regular activity of the imaging and pathology service; therefore, they did not constitute an additional expense for the participants.

Availability of data and materials

Data are available upon request to the corresponding author. No other materials are reported.

Author contributions

Rodrigo Fabian Díaz Pérez: conceptualization, validation, visualization, methodology, project administration, writing: review and edition.

Johana A. Arriciaga Vázquez: conceptualization, data curation, formal analysis, fundraising, research, resources, software, writing - original draft.

All authors read and approved the final version of the manuscript.

Ethics committee approval

It does not apply to observational studies.

Consent for publication

It does not apply when the patients' images, X-rays, or tomographies are not published.

References

1. Sood R, Rositch AF, Shakoor D, Ambinder E, Pool KL, Pollack E, Mollura DJ, Mullen LA, Harvey SC. Ultrasound for Breast Cancer Detection Globally: A Systematic Review and Meta-Analysis. J Globe Oncol. 2019 Aug;5:1-17. DOI: 10.1200/JGO.19.00127. PMID: 31454282; PMCID: PMC6733207.

2. Sannachi L, Gangeh M, Tadayyon H, Gandhi S, Wright FC, Slodkowska E, Curpen B, Sadeghi-Naini A, Tran W, Czarnota GJ. Breast Cancer Treatment Response Monitoring Using Quantitative Ultrasound and Texture Analysis: Comparative Analysis of Analytical Models. Transl Oncol. 2019 Oct;12(10):1271-1281. DOI: 10.1016/j.tranon.2019.06.004. Epub 2019 Jul 17. PMID: 31325763 ; PMCID: PMC6639683.

3. Thigpen D, Kappler A, Brem R. The Role of Ultrasound in Screening Dense Breasts-A Review of the Literature and Practical Solutions for Implementation. Diagnostics (Basel). 2018 Mar 16;8(1):20. DOI: 10.3390/diagnostics8010020. PMID: 29547532; PMCID: PMC5872003.

4. Freer PE. Mammographic breast density: impact on breast cancer risk and implications for screening. Radiographics. 2015 Mar-Apr;35(2):302-15. DOI: 10.1148/rg.352140106. PMID: 25763718.

5. Rebolj M, Assi V, Brentnall A, Parmar D, Duffy SW. Addition of ultrasound to mammography in the case of dense breast tissue: systematic review and meta-analysis. Br J Cancer. 2018 Jun;118(12):1559-1570. DOI: 10.1038/s41416-018-0080-3. Epub 2018 May 8. PMID: 29736009; PMCID: PMC6008336.

6. Uchida M, Gatica C, Hasson D, Gallegos M, Pinochet MA. Breast adenomyoepithelioma from a radiologic perspective. Radiology (English Ed). 2022 Mar;64 Suppl 1:37-43. DOI: 10.1016/j.rxeng.2021.06.004. PMID: 35428465.

7. Badu-Peprah A, Adu-Sarkodie Y. Accuracy of clinical diagnosis, mammography and ultrasonography in preoperative assessment of breast cancer. Ghana Med J. 2018 Sep;52(3):133-139. DOI: 10.4314/gmj.v52i3.5. PMID: 30602798; PMCID: PMC6303551.

8. Luo ST, Cheng BW. Diagnosing breast masses in digital mammography using feature selection and ensemble methods. J Med Syst. 2012 Apr;36(2):569-77. DOI: 10.1007/s10916-010-9518-8. Epub 2010 May 14. PMID: 20703679.

9. Destounis S, Arieno A, Morgan R. New York State Breast Density Mandate: Follow-up Data With Screening Sonography. J Ultrasound Med. 2017 Dec;36(12):2511-2517. DOI : 10.1002/jum.14294. Epub 2017 June 28. PMID: 28656638.

10. von Euler-Chelpin M, Lillholm M, Vejborg I, Nielsen M, Lynge E. Sensitivity of screening mammography by density and texture: a cohort study from a population-based screening program in Denmark. Breast Cancer Res. 2019 October 17;21(1):111. DOI: 10.1186/s13058-019-1203-3. PMID: 31623646; PMCID: PMC6796411.

11. Dilhuydy MH. Seins denses et dépistage organisé: place de l'échographie [Assessment of the dense breast within the French screening program: the role of ultrasonography]. J Radiol. 2008 Sep;89(9 Pt 2):1180-6. French. DOI: 10.1016/s0221-0363(08)73928-3. PMID: 18772802 .

12. Ghosh K, Brandt KR, Reynolds C, Scott CG, Pankratz VS, Riehle DL, Lingle WL, Odogwu T, Radisky DC, Visscher DW, Ingle JN, Hartmann LC, Vachon CM. Tissue composition of mammographically dense and nondense breast tissue. Breast Cancer Res Treat. 2012 Jan;131(1):267-75. DOI: 10.1007/s10549-011-1727-4. Epub 2011 August 30. PMID: 21877142; PMCID: PMC3707294.

Editor's Note

Revista Oncología Ecu remains neutral concerning jurisdictional claims in published maps and institutional affiliations.