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Enhancing mammographic screening quality: the impact of independent double reading in low- and middle-income countries

Abstract

Purpose: To evaluate the impact of independent double reading in a cohort of 5,000 consecutive women who underwent mammography. Results: Among the 5,000 mammograms reviewed, 68% presented no significant abnormalities. Multivariate analysis revealed that all evaluated imaging features had odds ratios (OR) greater than 2, with breast density (OR=8.239), microcalcifications (OR=23.481), and focal asymmetries (OR=10.052) showing the strongest associations with discrepancies. Conclusion: Independent double reading is a critical component of mammography screening quality assurance, particularly in low- and middle-income countries. Arbitration by a third expert further minimizes diagnostic errors, especially in dense breast tissue and subtle imaging findings.

Keywords: Mammography, quality control, screening, guidelines, breast cancer.

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Introduction

Breast cancer represents a significant global public health challenge, with a profound impact on women's health and well-being. In 2022, it was the most frequently diagnosed cancer among women, accounting for approximately 2.3 million new cases worldwide.[1] It is also the leading cause of cancer-related deaths in 12 world regions, most of them in low- and middle-income countries (LMICs).[2,3] In Brazil, breast cancer is the most common cancer among women, with an estimated 73,000 new cases annually (31.1%)[4] and remains the leading cause of cancer mortality among women.[5]

Mammography is globally recognized as the standard imaging modality for breast cancer screening. Numerous studies have demonstrated its efficacy in reducing both mortality and morbidity associated with advanced-stage disease.[6–8] However, the Canadian National Breast Screening Study (CNBSS) raised concerns when it reported no significant difference in breast cancer–related mortality between screened and unscreened women over a 25-year period. The study has been widely criticized for methodological limitations, particularly poor image quality.[9]

The effectiveness of regular mammographic screening for breast cancer-related mortality is having uncountable arguments favoring the maintenance and implementation of screening programs.[10–12] However, to achieve the greatest potential effects of such screening, it is necessary to ensure early access to effective diagnostic and treatment services. Successful implementation depends on timely access to diagnosis and treatment and robust quality assurance mechanisms to balance benefits and potential harm.[13]

Most of the breast cancer screening limitations are related to a number of variables that includes quality of the equipment used, training of the medical doctors in charge of the image analyzes, as well as nurses and physics technicians involved with equipment calibration, and an organized system for quality assurance of all procedures related to the mammography examination.[14,15] The main challenges of good practices and desirable efficacy of breast cancer screening also comprise the relatively low rates of cancer in a large volume of mammograms, the variable and subtle appearance of breast cancer, the great variation in breast density and the variety of normal breast tissue appearance; breast positioning, patient communication and quality control are likewise crucial issues that can affect mammography performance.[16] However, many LMICs do not have the mandatory infrastructure to ensure high-quality mammography and subsequent follow-up care, which critically impair the potential usefulness of mammogram examination.[17]

To improve diagnostic accuracy and reduce false-positive and false-negative rates, our institution implemented a comprehensive quality control system, including independent double reading of selected cases.[14] The mammography quality control program includes regular clinical (positioning), medical (reporting), and technical (equipment) evaluations based on national and international protocols, with a 20% sample of the total production reviewed by highly trained and qualified radiologists, medical physicists, and technologists. The program assesses both professional and equipment performance and incorporates AI-guided double reading to ensure diagnostic excellence and patient safety. Double reading is a standard practice in many European screening programs,[18] but is often considered infeasible in LMICs due to high associated costs.

This study aims to evaluate the impact of independent double reading on the accuracy of mammographic screening in a consecutive cohort of 5,000 women within a Brazilian healthcare service.

Materials and methods

This study analyzed 5,000 mammograms performed consecutively in 2015 as part of the breast cancer screening routine at the Department of Cancer Prevention of a Brazilian healthcare service.[14]

All mammograms were acquired using a GE Digital Mammography System (Senographe Essential, USA). Image analysis was performed on Dell workstations equipped with Hologic SecurView® software and 5-megapixel resolution monitors.

The radiologists responsible for image interpretation were extensively trained at the LRCB (Dutch Expert Centre for Screening) in the Netherlands and had broad experience in screening programs and mammographic quality control.

As part of the institutional quality control protocol, 5% of each radiologist's mammography reports were randomly selected for independent double reading (blind review). In cases of significant discrepancy between the two readers, a third radiologist conducted an arbitration reading to establish the final assessment. Based on the third evaluation, patients were either recalled or not, depending on the final classification.

The morphological variables analyzed were: mammographic density (adipose tissue, predominantly adipose tissue, predominantly dense or dense), regular nodule, irregular nodule, microcalcifications, architectural distortion, focal asymmetry. Cases were divided into Concordant and Discordant. Discordant cases were subdivided in significant and not-significant discrepancies. Arbitration for a third reader was performed on cases of significant discrepancies. After the third evaluation, women were recalled or not recalled, depending on the final judgment released by the third reader.

Statistical analysis

Mammography data were extracted from the hospital's Picture Archiving and Communication System (PACS – Pixeon). Data processing, multivariate data analysis, and image processing were performed using SPSS Statistics 20.0.1 (IBM Corporation, Somers, NY, USA).

Logistic regression was applied to identify the variables significantly associated with discordant readings. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. A p-value of <0.05 was considered statistically significant.

Results

The study cohort comprised 5,000 women aged 27 to 84 years (mean age: 52 years; median: 51 years), who underwent mammographic screening, with or without clinical breast symptoms. Independent double reading of 5% of reports per radiologist encompassed all 5,000 exams. Among these, 68% of cases presented no significant abnormalities. However, microcalcifications, focal asymmetries, and architectural distortions were identified in approximately 5% of the exams. Regular and irregular nodules were reported in 12% and 1% of cases, respectively. In 4% of cases, multiple findings were present. Regarding breast density, 59% of the cases were classified as predominantly dense tissue, while 27% were predominantly adipose. Figure 1 illustrates the decision flowchart for double and third-reader evaluations. Table 1 presents the multivariate logistic regression analysis, highlighting associations between imaging characteristics and the likelihood of discordant readings. All variables demonstrated odds ratios (OR) greater than 2, with the strongest predictors being microcalcifications (OR = 23.481, 95% CI: 14.788–37.282), focal asymmetry (OR = 10.052, 95% CI: 6.161–16.401), and dense breast tissue (OR = 8.239, 95% CI: 1.052–64.513). Table 2 summarizes the pathological findings from seven cases that, without double and third reading, would likely have been misclassified. These included ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC), with tumor sizes ranging from 0.5 to 3.0 cm and immunohistochemical profiles indicating ER+/PR+ status in most cases.

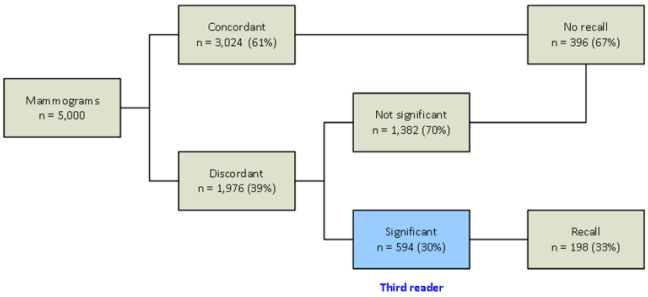

Figure 1 Flow chart of the double/third reading process.

Table 1 Multivariate data analysis of the image variables

	B	S.E.	Wald	p-Valor	O.R.	95% Confidence interval	
						Inferior	Superior
Adipose tissue			**11.018**	**0.012**			
Pred Adipose	1.286	1.041	1.526	0.217	3.619	0.47	27.844
Pred Dense	1.424	1.032	1.904	0.168	4.155	0.55	31.414
Dense	2.109	1.05	4.034	≤0.001	8.239	1.052	64.513
Regular nodule	1.152	0.225	26.22	0.045	3.165	2.036	4.918
Microcalcification	3.156	0.236	179.024	≤0.001	23.481	14.788	37.282
Distortion	0.861	0.37	5.401	0.02	2.364	1.144	4.886
Focal asymmetry	2.308	0.25	85.376	≤0.001	10.052	6.161	16.401

B, beta; SE, standard error; OR, odds ratio

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Table 2 Main findings detected by independent double reading system with arbitration by a third reader

	Histology	Nuclear grade	Tumor size (cm)	IHC	Lymph node status
Case 1	DCIS	II	3	ER +	-
Case 2	DCIS	III	1.3	ER +	-
Case 3	DCIS	III	0.7	ER +	-
Case 4	DCIS	II	0.5	ER +	-
Case 5	IDC	I	1.2	ER + / PR + / Ki67 +	0/1
Case 6	IDC	II	0.6	ER + / PR + / Ki67 +	0/1
Case 7	IDC	I	2.1	ER + / PR + / Ki67 +	0/3

CDIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; IHC, immunohistochemistry; ER, estrogen receptor; PR, progesterone receptor

Discussion

A major and persistent concern in breast cancer control is its increasing burden, particularly in developing and low-income countries, where medically underserved women bear the tragic consequences of public health inequities. The findings presented here clearly suggest that, even under optimal medical conditions, rigorous quality control in mammography is essential to ensure high diagnostic performance.

It is estimated that by 2020, 1.7 million new cases of breast cancer would be diagnosed in the developing world.[19] In Brazil, approximately 59,700 new cases of breast cancer were diagnosed in 2018, with an estimated incidence rate of 56.33 per 100,000 women.[20] In large countries such as Brazil, disparities in medical care are common, with some regions offering well-structured screening programs, while others fall short of international quality standards. Despite the high incidence of breast cancer in both developed and developing nations, survival rates differ significantly. Approximately 70% of breast cancer deaths occur in low- and middle-income countries (LMICs).[19] This discrepancy in mortality rates exists because the diagnosis of breast cancer in LMICs occurs predominantly at more advanced stages of the disease, increasing treatment-related morbidity, compromising quality of life and reducing patient survival.[20]

Low survival rates in LMICs are also linked to the scarcity of effective screening programs, the lack of adequate diagnostic and treatment services.[21] and delays in care delivery.[19] Cancer control in these settings is further hindered by weak healthcare infrastructure, competing health priorities, limited public awareness, uncontrolled exposure to carcinogens, insufficient funding, and shortages of trained healthcare professionals.[22]

Given these challenges, breast cancer represents a significant public health issue. As primary prevention remains largely unfeasible, efforts to promote early detection must be intensified.[19]

According to the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis, mammograms should be independently read by two radiologists—a practice known as double reading. This approach improves the sensitivity of screening by 5–15%[15]. However, double reading represents a substantial economic burden, especially in LMICs, and its cost-effectiveness in these settings is debatable.[23,24] In such contexts, a more feasible alternative could be targeted double reading for cases with high-risk clinical or radiographic features that warrant additional scrutiny. Indeed, our findings indicate that double reading significantly improves mammography quality. In our study, independent double reading with third-reader arbitration led to critical changes in clinical management, with seven cancer cases that could have been misclassified as benign being correctly identified.

Key mammographic features—such as microcalcifications, focal asymmetries, and dense breast tissue—were independently associated with higher rates of inter-reader disagreement. Recent studies confirm that blinded double reading can substantially improve cancer detection rates, albeit at the cost of increased recall and false positive rates.[25,26] Therefore, third-reader arbitration in cases of discordance can help enhance sensitivity while minimizing unnecessary recalls and improving positive predictive value.

The integration of artificial intelligence (AI) into mammography screening is a promising development. AI is being tested in various roles, including as a second reader, for triaging cases, aiding decision-making, and tailoring screening based on individual risk predictions.[27] The use of AI in mammography screening shows promising potential to reduce the workload associated with image interpretation and to improve cancer detection, which may ultimately enhance patient outcomes. However, these benefits must be validated through prospective studies, and any advantages should be carefully weighed against potential risks or unintended consequences.[18]

Some studies has shown that AI in screening scenario is promissory. The MASAI trial demonstrated that AI-assisted reading improved cancer detection by 29% and reduced radiologist workload without increasing recall or false positive rates.[28] However, the routine use of AI in LMICs is still limited by financial, logistical, and technical barriers.

It is important to recognize that mammography quality is influenced by numerous factors, including reading speed, suboptimal image resolution, and inadequate work environments. Specialized training should be provided to professionals who demonstrate a particular aptitude for mammographic interpretation, as this is key to reducing diagnostic error.[14,16] Avoiding misinterpretation is critical to ensuring the effectiveness of screening programs, and many studies have proposed strategies to improve the reliability of mammography results.[29–31]

The review process itself is nuanced. While non-independent double reading may improve sensitivity, it also increases recall. In contrast, independent double reading with consensus—or better, arbitration by a third reader—can enhance both sensitivity and specificity, albeit with a modest increase in cancer detection.[30] The main interpretive challenges lie in the subtle morphological details that must be accurately assessed to avoid false negatives and positives. Our data show that the presence of microcalcifications increases the likelihood of disagreement by 23.5 times. Focal asymmetries and dense breast tissue were associated with 10- and 8-fold increases in disagreement, respectively, compared to adipose tissue. Interestingly, combinations of these features did not significantly increase discordance rates beyond those observed with individual features.

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Double reading poses a significant challenge in LMICs due to limited resources and may be unfeasible in the poorest regions. However, selective independent double reading with third-reader arbitration for high-impact cases, as demonstrated in this study, along with investment in professional training, can sustainably improve screening quality. High-quality mammograms and well-trained radiologists are essential to the success of any screening program.[32]

In conclusion, independent double reading is a critical component of quality assurance in mammography screening, including in low- and middle-income countries. Arbitration by a third, experienced reader further improves diagnostic accuracy by reducing interpretation errors. Our findings highlight that microcalcifications, focal asymmetries, and dense breast tissue are independently associated with higher rates of disagreement among radiologists. Therefore, these features should be prioritized for secondary review in quality control processes. Despite the logistical and financial challenges associated with double reading, especially in resource-constrained settings, the selective application of this strategy—combined with targeted training and third-reader arbitration—can significantly enhance the effectiveness and reliability of breast cancer screening programs.

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Conflicts of interest

There authors declare no conflict of interest.

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