ORIGINAL REPORT

Impact of digital mammography in the detection and management of microcalcifications

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KEYWORDS
Mammography; Breast cancer; Breast cancer screening

Abstract

Objective: To determine whether the introduction of digital mammography in breast cancer screening has resulted in changes in the detection and management of microcalcifications.

\textit{Material and methods}: We retrospectively studied the performance indicators of our breast cancer screening program that are related to the diagnosis of microcalcifications (rates of recall and recommendation of intermediate follow-up after screening, rate of indication of invasive procedures for microcalcifications and their positive predictive value, detection rate for microcalcifications, and number of ductal carcinomas \textit{in situ} (DCIS) diagnosed). We compared the results obtained using direct digital mammography (September 2008–August 2009) with those obtained using analog mammography (September 2006–August 2007).

\textit{Statistical analysis}: Chi-square test and measures of association.

Results: We found that using digital mammography led to significant increases in the recall rate (from 50.8 to 64\%), in the rate of intermediate follow-up after screening (from 9.41 to 18.7\%), in the rate of indication for invasive procedures (from 1.88 to 3.01\%), in the cancers detected through microcalcifications (from 0.86 to 1.36\%), and in the number of DCIS diagnosed.

Conclusion: Direct digital mammography has improved the detection of microcalcifications, increasing the number of DCIS diagnosed without decreasing the positive predictive value of the invasive procedures indicated for microcalcifications. However, direct digital mammography has had a negative effect by increasing the recall rate and indication for short-term follow-up, possibly due to the difficulty of comparing the findings with those of earlier analog mammograms.

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PALABRAS CLAVES
Mammografía; Cáncer de mama; Detección precoz del cáncer

Influencia de la mamografía digital en la detección y manejo de microcalcificaciones

Resumen
Objetivo: Valorar si la introducción de la mamografía digital (MD) en el cribado del cáncer de mama ha supuesto cambios en cuanto a la detección y manejo de las microcalcificaciones.

Material y métodos: Se ha realizado un estudio retrospectivo de los indicadores de rendimiento de un programa de cribado del cáncer de mama que se relacionan con el diagnóstico de microcalcificaciones (tasas de recitación y de recomendación de controles intermedios después del cribado, tasa de indicación de procedimientos invasivos por microcalcificaciones, y su valor predictivo positivo, tasa de detección por microcalcificaciones y número de carcinomas ductales in situ [CDIS] diagnosticados). Se han comparado los resultados obtenidos con la mamografía digital directa (septiembre 2008-agosto 2009) frente a la mamografía analógica (septiembre 2006-agosto 2007). Para el análisis estadístico se utilizaron la Prueba de $\chi^2$ y medidas de asociación.

Resultados: Con MD se ha observado un aumento significativo de las tasas de recitación (de 50,8 a 64%), de realización de controles intermedios (de 9,41 a 18,7%), de indicación de pruebas invasivas (de 1,88 a 3,01%), de cánceres detectados por microcalcificaciones (de 0,86 a 1,36%) y del número de CDIS.

Conclusión: La MD directa ha mejorado la detección de microcalcificaciones incrementando el número de CDIS diagnosticados, sin disminuir el valor predictivo positivo de los procedimientos invasivos indicados por microcalcificaciones. Sin embargo, ha tenido un efecto negativo por el aumento en la tasa de recitación y de indicación de seguimiento a corto plazo, posiblemente debido a la dificultad de comparación con estudios analógicos anteriores.

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Introduction

Breast cancer is the most common cause of cancer-related deaths in women in Europe and represents a serious public health problem. Early detection through screening and the efficacy of current breast cancer therapies have helped to reduce mortality. In addition, advances in surgical treatment have contributed to a reduction in post-operative sequelae.

Mammography remains the modality of choice for early detection of breast cancer. Unlike in other fields of radiology, in mammography, digital technology took a longer time to be introduced in clinical practice and only in recent years has analog mammography started to be replaced by digital mammography in Radiology Departments and in Early Diagnosis Units. A number of studies have compared digital and analog mammography, and results suggest that digital mammography is at least as effective as analog mammography, both in clinical practice and breast cancer screening. In addition, full-field digital mammography has potential benefits compared to analog mammography, particularly in patients younger than 50 and in women with dense breasts. However, some studies show that the initial use of digital mammography may have some drawbacks, including the increase in false positives as a consequence of pseudolesions and increased detection of benign microcalcifications. The presence of microcalcifications is a relevant finding for early detection of breast cancer in asymptomatic women. Nevertheless, the spatial resolution of digital mammography may hinder the detection and characterization of microcalcifications.

The objective of this study is to determine whether the introduction of direct digital mammography in breast cancer screening has resulted in changes in the detection and management of microcalcifications.

Materials and methods

This study followed the protocols established for the access to the registry data of the results from the Breast Cancer Prevention Program of Navarra (Spain). Review of the clinical histories of the patients was not needed. Approval from the Ethics Committee was not requested since the results of the screening process were retrospectively reviewed.

Full-field direct digital mammography was introduced in the Breast Cancer Prevention Program of Navarra in September 2008 to replace the analog mammography systems. We retrospectively compared the results of the screening with direct digital mammography performed between September 2008 and August 2009 and the results obtained from a previous screening round with analog mammography performed on the same target population from September 2006 to August 2007. In all of the patients, the screening mammograms included a mediolateral oblique and a cranio-caudal projection, for both initial and subsequent screening examinations. Our study also included women who attended the program for the first time, as approximately 93% of them had undergone previous
mammographic screening. All the digital mammograms were performed with a Digital Loran Selenia mammography system (Hologic Inc; Danbury, USA), and the radiologists were familiar with the Computer Aided Detection (CAD) system (ImageChecker 9.0 RZ Technology Inc; Sunnyvale, USA). Mammograms were interpreted separately by four radiologists with one-year (one radiologist) and over twelve-year (three radiologists) experience in breast cancer screening. In order to maintain the recall rates and the criteria for referral for interventional procedures, some decisions were made by consensus. Our workstations are equipped with 5-megapixel monitors (Barco Coronis 5 MP Mammo; Brussels, Belgium), and comparisons were made with previous analog mammograms, which were available at the time of reading. All film mammograms were viewed on Rotalux M 680 negatoscopes (Planilux; Warstein, Germany).

The performance indicators recorded to evaluate the transition from analog to digital mammography were the following: number of women screened; recall rate (percentage of screened women who are referred for further testing after mammography—either extra mammographic views or ultrasonography); rate of intermediate or short-interval follow-up for microcalcifications after screening (proportion of women who are recommended a one-year follow-up instead of the standard two-year screening interval); referral rate for invasive procedures for microcalcifications and its positive predictive value; rate of microcalcification detection; and number of diagnosed ductal carcinomas in situ (DCIS).

The rates or percentages and 95% confidence intervals were calculated for these variables using exact methods (mid-p) and normal approximation (Wald). The χ² test and exact association measurements were used for comparison of results between analog and digital mammography. A p < 0.05 value was considered statistically significant.

Results

Table 1 shows the results from analog and digital mammography. The number of women screened by digital and analog mammography was 38,264 and 41,874, respectively.

The recall rate for additional tests was 64% in women screened with digital mammography and 50.8% in women screened with analog mammography (significant differences p < 0.001).

The rate of intermediate follow-up examinations for microcalcifications was 18.7% in women screened with digital mammography compared with 9.41% in women screened with analog mammography for the recommended follow-up at one year (significant differences p < 0.001).

The rate of referral for breast interventional procedures (in most cases, vacuum-assisted biopsy for microcalcification) was 3.01% with digital mammography and 1.88% with analog mammography (significant differences p = 0.002).

The positive predictive value of the interventional procedures was for microcalcifications was 47% for digital mammography, and 50.7% for analog mammography (non-significant differences p = 0.698).

The rate of tumor detection for microcalcifications also increased from 0.86% with analog mammography to 1.36% with digital mammography (significant differences p = 0.033).

The number of DCIS detected also increased from 17 with analog mammography to 34 with digital mammography (significant differences p = 0.007).

Discussion

Our study shows that the replacement of analog mammography with digital technology has had an impact on some of the performance indicators used to evaluate screening outcomes. Digital mammography has shown to be more sensitive in detecting microcalcifications, resulting in an increased number of diagnosed breast cancers. The negative effect of digital mammography is the increase in recall rates.

Direct digital mammography has several advantages over analog mammography, including a reduction in radiation dose; electronic image storage, which facilitates comparison with previous studies and the use of tools to optimize detection (contrast manipulation, zoom and computer-assisted diagnosis systems) (Figs. 1A–B and 2).
In the near future, digital breast tomosynthesis will likely become a major advance in early diagnosis allowing the detection of tumors that are occult to conventional mammography.13

Digital mammography was approved for clinical use in 2000 by the Food and Drug Administration (FDA), but it was not introduced in screening programs as easily as it was first thought. This was partly due to its high cost and to the initial doubts concerning its lower spatial resolution.13–15 The high cost and maintenance of direct digital mammography systems, as well as the fear that they would soon become obsolete, reduced the sales.16 Today, however, digital mammography is gradually replacing analog mammography in both clinical practice and early diagnosis programs.13

Some studies argue that the initial use of full-field digital mammography may increase the number of false positives as a consequence of pseudolesions and the detection of benign microcalcifications.8 In addition, because of its superior contrast resolution, a digital mammogram can falsely give the impression that a cluster of microcalcifications is new or has grown when compared with a previous analog image.17 This could be a problem especially in screening programs targeting large populations of asymptomatic patients, since the increase in false positives is one of the major drawbacks of digital mammography.18 Pseudolesion interpretation increases the number of recalls for further projections and/or ultrasonography. The increased detection of microcalcifications is accompanied by an increased number of referrals for biopsy, which would only be justified if more carcinomas were diagnosed.

As in previous studies,1,17 we also found a higher recall rate, which could be explained by the learning curve effect associated with the introduction of a new imaging tool and by the difficulty in comparing digital mammograms with analog mammograms of previous studies. Bluekens et al.17 report that the recall rate remained high not only during the first period, but also for two years. Therefore, this increase was due not only to the learning curve but also to the difficulty in comparing with previous studies. For this reason, we argue that our recall rate could be reduced to analog mammography levels in the next screening round, when the comparison will be made with digital mammograms.

Another drawback observed in our study is the increased number of women referred for a shorter interval follow-up screening. Guidelines recommend screening every two years.18 In accordance with the recommended standards, short-interval follow-up should be avoided to the extent possible because it increases the number of examinations and could be a source of anxiety in some patients. As with the overall recall rate, we argue that the high rate of short-interval follow-up is likely to stabilize to analog mammography levels in the next screening round, once the initial learning curve is passed and digital mammograms are available for comparison.

Regarding the assessment of microcalcifications, we also found an increase in the detection by digital mammography that led to a high referral rate for interventional procedures (without decreasing the positive predictive

Figure 1  (A) Analog mammogram shows a cluster of microcalcifications in the retroareolar region of the left breast that are difficult to visualize. (B) Detailed photograph of the cluster of microcalcifications in the retroareolar region that have remained stable for years.

Figure 2  Follow-up digital mammogram. In some cases, zooming facilitates the assessment of microcalcification morphology.
value of the invasive tests). The higher detection rate with digital mammography has also been reported in the literature.\(^5,6,9\) Karssemeijer et al.\(^6\) reported an increased recall rate based on microcalcifications and on a significant increase in DCIS detection. The use of digital mammography decreases the influence of breast density, thus facilitating the detection of microcalcifications. For this reason, we believe that some of these microcalcifications detected on digital images were likely to be already present in previous analog mammographic images; however, very often it is difficult to determine their presence and morphology because of the high density of breast tissue. Our study has also reported a significant increase in DCIS detection.

One of the limitations of our study is that the impact of the use of CAD on the increase in the detection of microcalcifications has not been evaluated. In addition, the influence of the learning curve on the outcomes was not evaluated, particularly in the case of the least experienced radiologist. Finally, due to the way our program collected the data, the recall rate reported is an overall rate, which includes all types of recall and not just those recalls made for microcalcification evaluation.

In conclusion, direct digital mammography appears to be more sensitive than analog mammography in the detection of microcalcifications, thus increasing the cases of cancers diagnosed. However, the positive predictive value of the invasive tests indicated for microcalcifications was similar to analog mammography values, despite the fact that an increase in the absolute number of false positives was observed. The results presented in this study suggest that digital mammography is more suitable for screening in the case of microcalcifications because it would increase the proportion of cancers detected without decreasing the efficiency of the program regarding diagnostic confirmation.

In addition, the negative effect of the introduction of digital mammography in our screening program was an increase in the rates of overall recalls and referrals for short-interval follow-up. This increase may be due to the difficulty in comparing with previous studies.

**Authorship**

1. Responsible for the integrity of the study: MM.
2. Conception of the study: MM, AO.
3. Design of the study: MM, AO.
4. Acquisition of data: AM, RB, AB.
5. Analysis and interpretation of data: MM, AO, MJP, NE.
6. Statistical analysis: MM, MJP, NE.
7. Bibliographic search: MM, RB, AB.
8. Critical review with intellectually relevant contributions: AM.
9. Writing of the paper: MM, AO, MJP.
10. Approval of the final version: MM, AO, AM, RB, AB, MJP, NE.

**Conflicts of interest**

The authors declare not having any conflict of interests.

**References**

