FALSE NEGATIVES IN MAMMOGRAPHY

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Abstract

The concept of false negative in mammograms is defined and the factors which can define its occurrence are exposed. Mechanisms which can be used to reduce its incidence are indicated.

There are six factors implied in false negatives: radiological anatomy of the breast, radiological characteristics of the lesion itself, performance of the radiology doctor, state of the equipment, performance of the radiology technician, and environment in which the process is developed.

To reduce the frequency of false negatives, the following procedures must be considered: imaging quality control, working team training, (including the doctor, technician and the rest of the people involved in the process of diagnosis), double reading of the images and computer aided detection.

Analyzing false negative causes should be a frequent practice in every center since this knowledge allows us to take steps to reduce the probability of their occurrence.

Keywords: false negatives, mammogram.


1) Introduction

Mammograms are the main tool in breast imaging and mammography is the only technique whose efficacy has been proved as screening test with the objective of detecting breast cancer before it is clinically evident.

Most scientific societies associated to mastology recommend performing a screening mammogram once a year after reaching 40 years of age.

A reduction in breast cancer mortality of at least 30 % achieved by using mammography screening has been proved.

In spite of what was previously mentioned, it is also a known fact
that mammograms do not detect all cancers.

There are cancers which are not perceived in a mammography and which later are manifested as interval cancer (before the set date for the following mammography control).

In this work we refer to a subject of great importance to breast imaging practice: false negatives in mammography.

We will describe several factors which can determine a false negative result and finally we will mention which mechanisms can be used to reduce the probability of its occurrence.

2) Definition

According to the text in the Breast Imaging Reporting and Data System (BI-RADS) developed by the American Radiology College (1), false negative in mammography is defined as the diagnosis of breast cancer during a period of up to one year after a mammography catalogued as negative.

All cases included in categories 1, 2 and 3 of BI-RADS are considered as a false negative mammography.

There is great variability in scientific publications regarding the frequency of false negatives.

Values of false negative rates from 4 to 34% have been published, but in most cases an occurrence of 10 to 20% (2, 3) is handled.

3) Implications of false negatives in clinical practice.

If a follow up of the development of breast cancer is carried out, it could

Figure 1.- Analisis of the factors related to false negative results in mammograms.
be observed that initially it goes through a stage in which it is not detectable by any method, then it goes through a stage in which it could be detected by imaging techniques such as mammograms and finally it enters the stage in which it is clinically evident. If the opportunity to detect it in the subclinical or imaging stage is missed, it will be later on detected by its clinical manifestations.

This delay in diagnosis can determine an unfavorable evolution since size in the moment of diagnosis is an important prognosis factor.

If the tumor has more time to develop, systemic dissemination will be more likely.

There may also be medical and legal consequences for the doctor responsible for the mammography report in which the error occurred.

Failure to detect breast cancer is the principal cause for suits against imaging doctors and one of the main causes for suits in medicine practice (4-6).

4) Causes of False negatives in mammography:

In order to understand why false negatives take place it is necessary to know that mammographic diagnosis is a process in which multiple factors interact and which are influenced by circumstances which may act as failure inducers.

Figure 2. - 38 years old female. A) mammography shows high radiological density parenchyma without evident lesions. B) Complementary ultrasound study shows an irregular solid mass of 20mm of diameter. Pathology confirms a ductal infiltrant carcinoma.
There are 3 types of failures which determine the occurrence of a false negative:

- The lesion is not visible in the image
- The lesion is visible in the image but not detected
- The lesion is detected but it is wrongly interpreted.

To analyze the factors which interact in the diagnostic process and the failure inducers it is useful to resort to an Ishikawa diagram or “fish bone” diagram. (fig. 1)

In this diagram we can observe that the implicated factors are 6:

- Radiological breast anatomy
- Radiological characteristics of the lesion itself
- Performance of the radiology doctor
- State of the equipment
- Environment in which the process develops.

Figure 3 – A) Mamograms without Eklund’s technique. B) After Eklund’s technique was used a mass in the right breast, that was not identified, appears.
a) Radiological breast anatomy:

High radiological density and the presence of implants or previous surgery are circumstances that can act as failure inducers. It is important to highlight the effect of high radiological density of the breast, which reduces the ability to detect lesions.

According to the American College of Radiology (1) the radiological density of the breast can be classified in 4 categories:

- ACR 1: breasts with adipose structure
- ACR 2: breasts with some dispersed fibro-glandular densifications.
- ACR 3: breasts with heterogeneously dense mammary tissue.
- ACR 4: extremely dense breasts.

There are studies which analyze the sensitivity of the mammogram in relation to breast radiological density (7, 8).

In its results it can be observed how sensitivity is notoriously reduced while radiological density increases.

The sensitivity of the mammogram is very low when breasts have maximum radiological density (ACR 4).

This explains the need to carry out supplementary ultrasound in the case of breasts with high radiological density, which allows us to detect lesions not visible in the mammogram.

In figure 2 we show the case of a 38 year-old patient’s mammogram with breasts of very high radiological density.

Ultrasound detected a solid 20 mm mass in the right breast, which was an infiltrating ductal carcinoma that was not perceived in the mammographic image.

Silicon implants may also affect the sensitivity of the mammogram since there may be sectors of the breast parenchyma, which may be hidden due to the high radiological density of silicon. This is more likely when the implants have been placed in front of the major pectoral muscle since the technique which allows us to separate breast tissue from the implant during the mammogram becomes difficult. This is the technique described by Eklund that consists in pushing back the implant to compress only the breast tissue, which becomes exposed to x-rays. (9)

Which ever the topography of the implants it is necessary to perform this technique to include in the image the biggest possible volume of breast tissue.

In figure 3 we show a case in which mammography performed with Eklund’s technique detected a mass in the right breast, which was not visible in the projections in which the mentioned technique was not performed.
b) Radiological characteristics of the lesion:

Regarding failure inducers associated to the lesion itself, size is of influence since the smaller is the lesion it is more likely that it will not be detected.

Some lesions are located in areas difficult to evaluate in the mammogram.

Lesions with a similar radiological density to the normal parenchyma are more difficult to detect.

Finally, there are cancers with radiological characteristics which suggest they are benign. These cancers usually have well-defined margins due to the absence of a desmoplastic reaction, they do not have calcifications or they cause a minimal distortion of normal structures.

Lesions with characteristics which suggest benignancy are grouped in category BI-RADS 3 and are named as lesions which are probably benign.

For these lesions an imaging follow up is usually recommended every 6 months during 2 years, to evaluate its stability. It is stated that even if they are correctly categorized up to 2% of these lesions are in fact a cancer.

A solid well-defined mass (figure 4), round group of micro calcifications and focal asymmetrical density are included in this category.

c) Performance of the radiologist.

Multiple failure inducers are acknowledged in the radiologist’s performance. These can reside in his training, the method used to analyze images or in limitations characteristic of human perception.

We must mention that the most frequent cause of false negatives in any imaging technique, including mammograms, is a mistake of the radiologist. It should also be emphasized that there is no radiologist who has not given an erroneous diagnosis in some opportunity.

Figura 4 – A solid well-defined mass without calcifications. BI-RADS 3

An error can happen due to omission, which is to say due to not detecting the lesion visible in the image or due to an erroneous interpretation. There are several circumstances which can act as error inducers. A distraction can also
be caused among other reasons by fatigue, work overload or an inappropriate environment.

An error can be caused by an inadequate methodology in the analysis of the images: not comparing with previous studies, lack of knowledge of clinical data or by not using an ultrasound as a complement in cases when it is necessary. There are errors caused by limitations characteristic of human perception. These mistakes can not be eliminated and all of us will make them at some stage (10, 11)

There are errors named alliterative which occur when the doctor who analyses an image allows him or herself to be influenced by a previous erroneous interpretation carried out by another doctor or by him or herself.

In figure 5 we observe the example of a mass with most of its contour very well defined but there is a sector which is hard to evaluate due to superposition of structures or the presence of irregularities.

In this case an adequate methodology requires additional projections and localized compression to eliminate superposed structures to enable a more detailed view of the complete contour of the lesion. If this methodology is not followed the case can result in a false negative.

A lesion visible in the mammogram in a sector of the breast can capture all our attention and cause us to forget to analyze the rest of the breasts. If we make this mistake, which is called “tunnel vision” or “satisfaction of search” we could omit another suspicious lesion located in another region of the same breast or the contro-lateral breast.

**Figure 5- Nódulo con parte se sus márgenes ocultos por el tejido circundante. Requiere proyecciones adicionales**

**d) State of the equipment**

Regarding the equipment, it is of interest how old it is, its maintenance and control of its quality. In each center there should exist protocols for quality control where the tasks of each person involved should be defined. Each center should count with the participation of a medical physicist in the process to control equipment quality.
e) Performance of the imaging graduate.

Regarding the performance of the imaging graduate (radiology technician), an inadequate positioning of the patient during the mammogram is acknowledged as the main failure inducer in mammography.

These errors may determine that the lesion is not adequately visible in the image. This event is usually associated with a lack of training or work overload.

In these cases the doctor must request that the study is repeated and should indicate the mistakes made. The most common consequences in positioning errors are:

- Retro mammary adipose tissue is not included in the cranio-caudal projection.

- Lateral external or internal sector of the mammary gland is not included in the cranio-caudal projection.

- Pectoral muscle or the sub mammary crease is not included correctly in the oblique projection. We stress that in this projection the pectoral muscle must be seen up to half the image, with the anterior convex border forward and the sub mammary crease must be extended.

In figure 6 we can observe an example of a mammogram in which due to the incorrect positioning of the patient, the sub mammary crease is not visualized adequately. When the error is corrected a lesion located in the sub mammary crease of the right breast becomes visible.

f) Environment in which the diagnosis is carried out.

The environment in which the diagnosis is carried out can generate failure if there are conditions, which provoke distractions, such as: annoying noise, people walking around or visualizing conditions that are inadequate.

5) Measures to reduce the probability of false negatives.

We should stress that it is not possible to completely eliminate false negatives due to the great number of factors involved, but that it is possible to adopt measures which tend to reduce the probability that they occur.

The following procedures should be considered:

- Controlling image quality
- Training of the working team, including the doctor, the technician and the rest of the people involved in the process of diagnosis.
- Double reading of the images.
- Computer aided detection.

To achieve a high quality mammogram, a quality control and guaranty program must be followed which includes specific tests for each stage of the process.
The responsibilities of each member of the working team whether they are doctors, technicians or medical physicists, must be specified. Specifically trained in breast imaging with a group who had. (12). They observed that in the first case the sensitivity of the diagnosis is maintained over the years below the levels recommended by the Healthcare Research and Quality Agency.

In the group of doctors with specific training in breast imaging the desired sensitivity values were reached after two years of practice and they were maintained over the years.

In the regulations of Mammography Quality Standards Acts (13), the following are stated as initial requisites for the doctor who interprets mammograms:

There should also exist a firm compromise on the part of the center’s management, since without investment high quality is not possible.

It must be understood that high quality is achieved by team work where each member must assume the corresponding responsibilities.

The radiologist’s training clearly influences the results.

Migliorreti and Cols compared the performance of a group of imaging doctors who had not been specifically trained in breast imaging with a group who had. (12). They observed that in the first case the sensitivity of the diagnosis is maintained over the years below the levels recommended by the Healthcare Research and Quality Agency.

In the group of doctors with specific training in breast imaging the desired sensitivity values were reached after two years of practice and they were maintained over the years.

In the regulations of Mammography Quality Standards Acts (13), the following are stated as initial requisites for the doctor who interprets mammograms:
- Corresponding doctor and imaging specialist degrees
- A minimum of 3 months specific training in mammography which must include:
  o Training in medical physics
  o A minimum of 240 mammograms interpreted under supervision, which includes report, discussion and diagnostic confirmation.
  o A minimum of 60 hrs of continuous medical education which includes subjects of anatomy, physiology, pathology, technique, radio physics and quality control.

Permanent requisites will be:

- Continuous medical education
- Minimum of 960 mammograms interpreted every 24 months with the aim of not losing visual training when analyzing images.

It must be taken into account that quality control and training cannot eliminate errors associated to limitations pertaining to human perception.

Double reading techniques and computer aided detection were developed to reduce these errors.

Double reading is the method by which two or more radiologists interpret mammograms independently. This method can determine an increase in the rate of cancer detection of 5 to 15% (14). The method has the disadvantage of an increase in costs and an increase in false positives.

Computer aided detection is a system applicable to digital mammograms, in which there are marks superposed to the image which indicate the area of interest. The radiologist decides if the marked areas are of diagnostic value. This system determines an increase in the detection rate of cancer of 7 to 20% according to published works (15).

6) Conclusions:

In conclusion of the exposed, we must state that false negatives in mammography have a multi factor origin. It is important to understand where and how the failure which leads to a false negative can be generated. The analysis of failures can help us know our weaknesses and to learn from them. Using this knowledge, measures can be adopted to reduce the probability of their occurrence.
7) Bibliography:


