Evaluation of Micro-Calcification in Non-palpable Breast Lesions Detected by Screening Mammography in Correlation with Histopathology and Breast Cancer Risk Factors Distribution

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Abstract: The main purpose of this research was to evaluate the micro-calcification in non-palpable breast lesions detected by screening mammography in correlation with histopathology and breast cancer risk factors distribution. This study has been carried out as past-view over the cross-section areas of the micro-calcification among women along with strotactic biopsy. These patients have been also evaluated by the related method with 115 biopsy cases regarding to the mass of non-palpable micro-calcification that it has been merely represented in the field of conventional mammography during 2002-2008. The results showed in 61% patients, the number of the micro-calcifications is equal or higher than 5 numbers with 1mm diameter while these micro-calcifications could not be seen in the control group (p=0.020). The most common establishment of these micro-calcifications is out of the breast upper outer quadrant (35 out of 115, 30.5%). The most common shape of these micro-calcifications along with the pathological results is cluster type of cancer. About 69.5% patients reported BIRADS4 mammography. The most common risk factors of the breast cancer along with the pathological reports are the occurrence of the family background (50%), Noliparity (33%), the early pregnancy after 30 years old (33%); the most risk factor of these patients is subjected to cancer among 29.5% of the related patients (25out of 85) and other risk factors are the beginning of the menstruation age 20 out of 85 or 23.5%, family background for the breast cancer 17.5% or 15 out of 115 total population.

Keywords: Micro-Calcification, Breast, Mammography, Histopathology, Cancer.

Introduction

Mammography is one of the non-invasive methods that have been subjected to the evaluation of the breast. This can be also applied in both screening and discovery of the diseases as a suitable diagnosis (1). The secondary prevention of the cancer using the screening tests is subjected to the recognition of diseases in patients without any
symptoms for the early stages of the disease because the process of screening is applied in many individuals without any symptoms. The occurrence of the disease is usually established in low level and many individuals should tolerate the test positive signs if there is no established any symptoms; about 50% of the breast cancer is discovered in early stage through the process of mammography in this patients. The process of palpating can only discover about 20% of the related disease. In screening programs the physical evaluation of the breast and mammography is also applied for women without symptoms (Haghighatkahal et al., 2009).

The screening mammography for discovering the breast cancer is applied without any symptoms among women and it also is considered as the clinical evaluation. Two sections are obtained for every breast with the mammography. The mammography is the best method for seeking and recognizing the pre-mature cancer for the breasts. Usually, the mammography is achieved by two methods including the preparation of radiological usual films for being used in the process of screening and xeromammography (Berek, 2002). Diagnostically the breast cancer and the results for the same disorder are equal together for both related methods but more x-rays are applied in the second method. Mammography is the only authentic method for diagnosing the breast cancer before palpable fatal mass. Those breast cancers having slow growth and before reaching to palpable sizes in 2 years can be easily diagnosed by the mammography. The most common disorder is called the breast carcinoma in this process. It includes a collection of micro-calcifications in a mass in the breast; it sometimes appears as a mass without the calcification. The routine application of the screening in mammography can reduce the mortality between women ranging 50 years old and higher; this can be also effective for 33% of these women (Brunicardi et al., 2005). The mortality and morbidity of the breast cancer among women higher 50 years old has been considerably reduced for those women achieving the mammography although these screening methods are controversial discussions about women 40-49 years old. The US cancer institution suggests the mammography for women 40-49 years old in order to screen their disorders in these patients (Aghazadeh et al., 2001).

It is claimed that a skillful radiologist can find the breast cancer with 10% positive fake and 7% negative fake for the related disorder. The exclusive figures of the mammography represent the breast cancer including a mass with or without star-shaped figures, thickening the breast non-symmetrical culture and cluster-based micro-calcifications, a thin calcium into the breast and a tumor into its surrounding areas that consist more than 50% of the non-palpable cancers in this case. These micro-calcifications are the main symptoms of the cancer among women. It may be the only unusual finding of the mammography (Brunicardi et al., 2005). Achieving the most accurate mammography is very essential for finding the early stages of the breast cancer because it provides about 90% true existence of the cancer positively (Lawrence, Gerard, 2009).

Anyway, the mammography is the basic of screening the breast cancer. All mammography institutions recommend the routine screening for women higher 40 years old during 2 years. Of course the positive fake results of the process may restrict the pure and true benefit of the mammography. The digital mammography is very sensitive among young women that it mainly is suggested for breasts with mass (Tice & KerlikowskeK, 2007). The accidental future studies show a 40% reduction for steps 2, 3 and 4 regarding to the breast cancer among the screening population with 30% increase of women survive through the screening mammography (Lawrence & Gerard, 2009). Hence, the investigation of the found micro-calcifications during the screening mammography of the non-palpable masses and the adaptation of the pathological events and the distribution of the dangerous breast cancer factors have been carried out in this case.

Methods and Materials

This study has been carried out as past-view over the cross-section areas of the micro-calcification among women along with strotactic biopsy. These patients have been also evaluated by the related method with 115 biopsy cases regarding to the non-palpable micro-calcification that it has been merely represented in the field of conventional mammography during 2002-2008. The women without micro-calcification have been taken up in the observational group. Those women with palpable micro-calcification and other cases with structural distortions have not been included in this study. In all subjects these micro-calcifications have been shown by the mammography and a complete radiography evaluation is achieved on them efficiently. The available mammography films of these patients are compared with the latest mammography in order to achieve the related biopsy. The accuracy of the targeted tumors cases of the biopsy has been confirmed by the pathological studies. The pathologists evaluated all samples in order to diagnose the existence of the related micro-calcifications in every report. If no micro-calcification has been seen by these pathologists another biopsy or an excisional biopsy is also carried out on the related patients. The features of the mass based on the main mammography scans are investigated as retrospective in this case. The mean number of these micro-calcifications and the area of these into the breast as well as the
histopathological diagnosis have been again carried out in these patients. Then these were matched with the radiographic and histopathological reports. The mean diameter of these micro-calcifications measured based on their longitudinal dimension. The main risk factors of the breast cancer include the age of patient, beginning of early menstruation (12 years old), beginning of pregnancy after age of 30, taking anti-pregnancy drugs, and having breast cancer background of first degree family members and other cancers, as well as Nuliparity.

**Results**

**Figure 1.** Age group patients.

Figure 1 shows that the most common age groups of patients with non-palpable breast microcalcifications are age groups 41-50 and 51-60. This was followed in decreasing order by age groups 61-70 and groups 31-40 and 71-80.

**Figure 2.** First menses of the patients.

Figure 2 shows that the majority of patients had their first menses when they were 12 to 13 years old.
Figure 3. Microcalcifications of Patients.

Figure 3 shows that majority of patients (61%) detected with breast microcalcifications have equal to or more than 5 microcalcifications discovered. While the rest of the patients studied (39%) have less than 5 microcalcifications.

Figure 4. Location of breast microcalcification in patients.

Figure 4 shows that the most common location of the breast microcalcification detected was at the right upper outer quadrant area of the breast in the majority of patients (35.115, 30.43%)

Table 1. Breast cancer Risk Factors among Women

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Nuiparity</td>
<td>29.5%</td>
<td>33%</td>
</tr>
<tr>
<td>Age of Menarc before 12</td>
<td>23.5%</td>
<td>None</td>
</tr>
<tr>
<td>Family HX. Of Breast Cancer</td>
<td>17.5%</td>
<td>50%</td>
</tr>
<tr>
<td>Age of 1st Pregnancy after 30</td>
<td>17.5%</td>
<td>33%</td>
</tr>
<tr>
<td>OCP Usage HX</td>
<td>11.7%</td>
<td>None</td>
</tr>
</tbody>
</table>
The results of the study showed that most patients are established between 41-60 years old (30.4%) with 54.7% mean age. The menstruation age is ranging between 12-13 years old (52.17% and 60 cases of these patients 115). 85 patients out of 115 ones (73.9%) had pregnancy background and most of these patients had early pregnancy between 25-36 years old with 26.9 mean age. About 100 patients (87%) had never taken any anti-pregnancy drugs and 52% of the same patients had lactation background. The risk factors of the breast cancer (74% of patients) are taken place and found among 85 patients of 115 total subjects; it is established in a high number in compare to the control group significantly (P= 0.001). About 26% (30 out of 115 patients) had family background for the breast cancer that these are significant in compare to the control group (p=0.042).

In most patients (61%), the number of the micro-calcifications is equal or higher than 5 numbers with 1mm diameter while these micro-calcifications could not be seen in the control group (p=0.020), the most common location of these micro-calcifications is in the outer upper quadrant (35 out of 115, 30.5%). The morphology of these micro-calcifications about 65 out of 115 or 56.6% being seen as cluster-shaped cases. Other morphologies include cluster and pleomorphic in 25 cases or 21.7%, pleo-morphic in 15 cases or 13% and the rest are dotted and amorphus. The most common shape of these micro-calcifications among the patients with malignant pathologic results is cluster type, 18 out of 30 patients (60%), 80 patients out of 115 (69.5%) reported with BIRADS4 mammography. This malignancy is seen among 30 patients with non-palpable micro-calcification (26%) representing the positive predictive value of 26% malignancy for the related disorder.

The most common risk factors of the breast cancer in the patients with malignant pathologic reports are the occurrence of the family background (50%), Noliparity (33%), the early pregnancy after 30 years old (33%); and in the patients with benign pathologic result were nulliparity 25 out of 85 benign patient or 29.5% , and other risk factors are the beginning of the menstruation age 20.85 or 23.5%, family background for the breast cancer 17.5% or 15 out of 115 total population, early pregnancy after 30 years old 17.5% and the background of taking anti-pregnancy drugs 11.7% or 10 out of 85 subjects. A one-third of these patients with the malignant pathological results had 3 risk factors; 17% (5out of30) had a one risk factor and 50% were without any risk factors. 67% of these patients showed the malignant disease according to BIRADS mammography report Class4 and 33% had BIRADS Class3.. Among the benign patients 70% had BIRADS4 and 24% had BIRADS5 and only 6% of them had BIRADS3. Among patients with BIRADZ4 about 15/75 or 20% had malignant cases and the rest indicated benign pathologic findings while the degree of malignancy occurrence among patients with BIRADZ5 is one-third or 33% (10/30). All patients with 3 risk factors had malignancy and the difference between these risk factors between control and the related group was significant statistically (p=0.01). None of the patients were malignant along with early age of the first menstruation; the malignancy is seen among one-third of the patients taking anti-pregnancy drugs (5.15). Malignancy was detected in 16% of patients with less than 5 micro-calcifications and 24% of the patients with more than 5 micro-calcifications.

**Table 2. Patients with the malignant/benign pathological results**

<table>
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<tr>
<th>Birads</th>
<th>Malig. Histopath. Results</th>
<th>Benign Histopath. Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>None</td>
<td>6%</td>
</tr>
<tr>
<td>IV</td>
<td>67%</td>
<td>70%</td>
</tr>
<tr>
<td>V</td>
<td>33%</td>
<td>24%</td>
</tr>
</tbody>
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**Discussion and Conclusion**

Today only 10% of women have shown the progressive breast cancer (Brunicardi et al., 2005); the breast cancer can involve all women in all ages, races, tribes and social classes and the geographical areas (Hoskins and Haber, 2000). In a study, the most malignant cases of the breast cancer are seen during forty and fifty decades respectively (Syna et al., 2002). The occurrence age of the breast cancer is 50 years in other countries (in Iran this reaches to 40 years old higher) (Shahnaizi et al., 2009). The results of our study showed that most of these patients are established between 41-60 years old (30.4%) and their mean age is 54.7 years old. The rapid evaluation of the breast problems among women is essential for avoiding in delay and removing the breast cancer among these women. By increasing the age, the degree of breast cancer outbreak will be also increased. The breast masses are commonly resulting from Fibro adenoma among adults (Smeltzer et al., 2008). 20% of these breast masses are
malignant among women ranging between 35-45 years old while this degree is 35% in women 55 years old and 85% of the breast masses are carcinoma among older than 55. The breast pain is one of the common complaints along with the breast mass that it should be carefully evaluated to rule out cancer in this regard (39%) (Aghazadeh et al., 2001). Diagnostic mammography is applied in order to evaluate women for having abnormal symptoms such as breast mass or nipple discharge (Lawrence and Gerard, 2006). In a study led by Mahouri et al there is found a significant relationship between the former background of the breast disease and the family background for the breast cancer (Mahoori et al., 2003). In a study led by Rotledge et al the mammography accompanied with higher risk of family history and disease background (13). In another study there is found a significant relationship between the breast benign mass and the family background of breast cancer (P<0.05). In our study about 26% (30.115) had family background of breast cancer and 35% (40 out of 115) had family history for other types of cancers. For the reason, it is necessary for all women to train all about the screening methods. The mammography and sonography are the most authentic techniques for early diagnosis of the breast lesions (Berek, 2002). In a study in the US during 14 years, the mammography screening of women higher 40 years old about 16% reduction is seen all about the mortality and morbidity of these women annually and this should be also carried out over women 50 years old and higher annually and this should be also carried out for women 40-49 biannually. In younger women with family history of breast cancer and background of breast disease the mammography is needed urgently for diagnosing the existence of the breast cancer, annually (Haghighatkhah et al., 2009). In a study led by Haghighat Khah et al for 170 mammography cases, about 73% malignant cases are reported in this regard. While in the study of Dowyouli the sensitivity of the mammography is reported 51.2% (Devullidish et al., 2009). Most cancers seen in the mammography pictures are composed of some structural distortions, masses, calcifications and or a combination of three types in this regard. The masses and calcifications are seen about 90% of the breast cancers. In masses with uncertain or ill-defined edges, thoughtness and micro-calcifications are seen indicating the possibility of the irregular malignancy in this regard.

While the round-shaped masses are likely benign in this case. The irregular masses indicate more malignant cases. The edges of the masses are the most important cases because these represent the adenoma diseases such as Fibro Adenoma or the existence of a cyst in this case while the other edges may show the existence of the breast malignancies. The micro-calcifications are the common mammographic findings and most of these are not related to the malignancy. If exist the appearance; place, number and distribution of them are very important in this case. The micro-calcification relating to the malignancy is established between 0.5-1mm and it may be very linear and branched type (Tice & Kerlikowske, 2009). In our study, most of these patients (61%) have equal or higher 5 numbers micro-calcifications with 1mm diameter. In this study, the most common establishment of these micro-calcifications is located in the upper outer part of the breast. The early discovery is coming along with the cancer prognosis. Hence this is every physician’s task and duty to make his or her diagnosis for the existence of the cancer (Kasper, 2005). The routine application of the mammography screening among women 40 years old can reduce the mortality and morbidity about 33% (Brunicardi et al., 2003). The process of the mammography is applied in North America since 1960s and the applied techniques have been also revised with better picture quality. The mammography screening is also used for the discovery of the cancer among women and it also is considered as a supplementation for the clinical diagnosis (Lawrence & Gerard, 2006). However another study did not confirm the breast cancer screening methods satisfactorily and for the reason there have been established a recommended some other methods for treating these events potentially (Farshbaf Khalili et al., 2009). Training people for getting away from the risky and dangerous factors is one of the most influential approaches for courage people to prevent any diseases in these patients. The risk factors of the cancer include the age, family background, early menarche, late menopause, first term delivery after 25 years old, Nulliparity and OCP use. In our study the most common risk factor among the malignant patients include the family background 50%, Nulliparity 33%, early postpartum after 30 years old in 33%. While the most risky factors among the benign patients were Nulliparity in 29.5% (25.85), low age of menstruation or early menarche (23.5%), family background of the breast cancer 17.5%, the first term delivery/pregnancy after 30 years old 17.5% and the background of taking anti-pregnancy drugs in 11.7%.

The mammography is a technique for determining and diagnosing the micro-calcifications. It can be also used as a modality for breast cancers pre-mature screening particularly in patients with non-palpable masses; of course it can be applied as a tool for specifying the cancer risks playing a key role for recovering and treating the cancer as a better prognosis.
References

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