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Comparative evaluation of diagnostic accuracy of mammography and ultrasonography in breast cancer patients from Bihar region

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Abstract
Mammography and sonography are the standard imaging techniques for detection and evaluation of breast disease. Mammography is the most established screening modality. Especially in young women and women with dense breasts, sonography appears superior to mammography, and differentiation between solid tumours and cysts is easier. Sensitivity and specificity of sonography or mammography are higher if sonography and mammography are combined. Hence based on above findings the present study was planned to evaluate diagnostic accuracy of mammography and ultrasonography in breast cancer patients.

The present study was planned in Department of Radio- Diagnosis, Narayan Medical College and Hospital, Sasaram, Bihar from Jan 2018 to July 2018. The 25 women's with breast lesions detected on clinical examination/self breast examination and referred for mammography and women in high risk groups (family history of breast cancer, previous history of breast cancer and disease like fibrocystic disease, excessive exposure to ionising radiation and history of endometrial, ovarian or colonic carcinoma.

Mammogram and ultrasonography are two important non-invasive investigations available for evaluating breast diseases. Mammogram is more efficient in diagnosing malignant diseases of the breast, whereas ultrasonography is more efficient in diagnosing benign breast diseases. The combinations of ultrasonography and mammogram will diagnose almost all diseases of the breast. In this study we confirm that ultrasonography when combined with mammography in detection of breast lesions has more specificity, sensitivity, and accuracy when compared to a single modality in detecting breast lesions.

Keywords: breast cancer, mammography, ultrasonography, etc

1. Introduction

Breast cancer is cancer that develops from breast tissue. Signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, a newly-inverted nipple, or a red or scaly patch of skin. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin.

Risk factors for developing breast cancer include being female, obesity, lack of physical exercise, drinking alcohol, hormone replacement therapy during menopause, ionizing radiation, early age at first menstruation, having children late or not at all, older age, prior history of breast cancer, and family history. About 5–10% of cases are due to genes inherited from a person's parents, including BRCA1 and BRCA2 among others. Breast cancer most commonly develops in cells from the lining of milk ducts and the lobules that supply the ducts with milk. Cancers developing from the ducts are known as ductal carcinomas, while those developing from lobules are known as lobular carcinomas. In addition, there are more than 18 other sub-types of breast cancer. Some cancers, such as ductal carcinoma in situ, develop from pre-invasive lesions. The diagnosis of breast cancer is confirmed by taking a biopsy of the concerning lump. Once the diagnosis is made, further tests are done to determine if the cancer has spread beyond the breast and which treatments are most likely to be effective [1].

The balance of benefits versus harms of breast cancer screening is controversial. A 2013 Cochrane review stated that it is unclear if mammographic screening does more good or harm. A 2009 review for the US Preventive Services Task Force found evidence of benefit in those 40 to 70 years of age, and the organization recommends screening every two years in women 50 to 74 years of age. The medications tamoxifen or raloxifene may be used in an effort to prevent breast cancer in those who are at high risk of developing it. Surgical removal of both breasts is another preventative measure in some high risk women. In those who have been diagnosed with cancer, a number of treatments may be used, including surgery, radiation therapy, chemotherapy, hormonal therapy, and targeted therapy. Types of surgery vary from breast-conserving surgery to mastectomy. Breast reconstruction may take place at the time of surgery or at a later date. In those in whom the cancer has spread to other parts of the body, treatments are mostly aimed at improving quality of life and comfort [2].

Outcomes for breast cancer vary depending on the cancer type, the extent of disease, and the person's age. Survival rates in the developed world are high, with between 80 and 90% of those in England and the United States alive for at least 5 years. In developing countries, survival rates are poorer. Worldwide, breast cancer is the leading type of cancer in women, accounting for 25% of all cases. In 2012 it resulted in 1.68 million new cases and 522,000 deaths. It is more common in developed countries and is more than 100 times more common in women than in men [3].

The first noticeable symptom of breast cancer is typically a

lump that feels different from the rest of the breast tissue. More than 80% of breast cancer cases are discovered when the woman feels a lump [18]. The earliest breast cancers are detected by a mammogram. Lumps found in lymph nodes located in the armpits can also indicate breast cancer.

Indications of breast cancer other than a lump may include thickening different from the other breast tissue, one breast becoming larger or lower, a nipple changing position or shape or becoming inverted, skin puckering or dimpling, a rash on or around a nipple, discharge from nipple/s, constant pain in part of the breast or armpit and swelling beneath the armpit or around the collarbone. Pain ("mastodynia") is an unreliable tool in determining the presence or absence of breast cancer, but may be indicative of other breast health issues [4].

Another symptom complex of breast cancer is Paget's disease of the breast. This syndrome presents as skin changes resembling eczema; such as redness, discoloration or mild flaking of the nipple skin. As Paget's disease of the breast advances, symptoms may include tingling, itching, increased sensitivity, burning, and pain. There may also be discharge from the nipple. Approximately half the women diagnosed with Paget's disease of the breast also have a lump in the breast [5]

. Inflammatory Breast Cancer presents with similar effects. Inflammatory Breast Cancer is a rare (only seen in less than 5% of breast cancer diagnosis) yet aggressive form of breast cancer characterized by the swollen, red areas formed on the top of the Breast. The visual effects of Inflammatory Breast Cancer is a result of a blockage of lymph vessels by cancer cells. This type of breast cancer is seen in more commonly diagnosed in younger ages, obese women and African American women. As inflammatory breast cancer does not present as a lump there can sometimes be a delay in diagnosis [6]

. In rare cases, what initially appears as a fibroadenoma (hard, movable non-cancerous lump) could in fact be a phyllodes tumor. Phyllodes tumors are formed within the stroma (connective tissue) of the breast and contain glandular as well as stromal tissue. Phyllodes tumors are not staged in the usual sense; they are classified on the basis of their appearance under the microscope as benign, borderline or malignant [7]

. Malignant tumors can result in metastatic tumors—secondary tumors (originating from the primary tumor) that spread beyond the site of origination. The symptoms caused by metastatic breast cancer will depend on the location of metastasis. Common sites of metastasis include bone, liver, lung, and brain [8]. When cancer has reached such an invasive state, it is categorized as a stage 4 cancer, cancers of this state are oftentimes fatal [9]. Common symptoms of stage 4 cancer include unexplained weight loss, bone and joint pain, jaundice and neurological symptoms. These symptoms are called non-specific symptoms because they could be manifestations of many other illnesses [10].

Most symptoms of breast disorders, including most lumps, do not turn out to represent underlying breast cancer. Less than 20% of lumps, for example, are cancerous [30], and benign breast diseases such as mastitis and fibroadenoma of the breast are more common causes of breast disorder symptoms [11].

Most types of breast cancer are easy to diagnose by microscopic analysis of a sample—or biopsy—of the affected area of the breast. Also, there are types of breast cancer that require specialized lab exams. Breast cancer, like other cancers, occurs because of an interaction between an environmental (external) factor and a genetically susceptible host. Normal cells divide as many times as needed and stop. They attach to other cells and stay in place in tissues. Cells become cancerous when they lose their ability to stop dividing, to attach to other cells, to stay where they belong, and to die at the proper time.

Normal cells will commit cell suicide (programmed cell death) when they are no longer needed. Until then, they are protected from cell suicide by several protein clusters and pathways. One of the protective pathways is the PI3K/AKT pathway; another is the RAS/MEK/ERK pathway. Sometimes the genes along these protective pathways are mutated in a way that turns them permanently "on", rendering the cell incapable of committing suicide when it is no longer needed. This is one of the steps that causes cancer in combination with other mutations. Normally, the PTEN protein turns off the PI3K/AKT pathway when the cell is ready for programmed cell death. In some breast cancers, the gene for the PTEN protein is mutated, so the PI3K/AKT pathway is stuck in the "on" position, and the cancer cell does not commit suicide [12].

Mutations that can lead to breast cancer have been experimentally linked to estrogen exposure [13]. Additionally, G-protein coupled estrogen receptors have been associated with various cancers of the female reproductive system including breast cancer. Abnormal growth factor signaling in the interaction between stromal cells and epithelial cells can facilitate malignant cell growth. In breast adipose tissue, overexpression of leptin leads to increased cell proliferation and cancer [14].

In the United States, 10 to 20 percent of people with breast cancer and people with ovarian cancer have a first- or second-degree relative with one of these diseases. The familial tendency to develop these cancers is called hereditary breast–ovarian cancer syndrome. The best known of these, the BRCA mutations, confer a lifetime risk of breast cancer of between 60 and 85 percent and a lifetime risk of ovarian cancer of between 15 and 40 percent. Some mutations associated with cancer, such as p53, BRCA1 and BRCA2, occur in mechanisms to correct errors in DNA. These mutations are either inherited or acquired after birth. Presumably, they allow further mutations, which allow uncontrolled division, lack of attachment, and metastasis to distant organs. However, there is strong evidence of residual risk variation that goes well beyond hereditary BRCA gene mutations between carrier families. This is caused by unobserved risk factors. This implicates environmental and other causes as triggers for breast cancers. The inherited mutation in BRCA1 or BRCA2 genes can interfere with repair of DNA cross links and DNA double strand breaks (known functions of the encoded protein). These carcinogens cause DNA damage such as DNA cross links and double strand breaks that often require repairs by pathways containing BRCA1 and BRCA2. However, mutations in BRCA genes account for only 2 to 3 percent of all breast cancers. Levin et al. say that cancer may not be inevitable for all carriers of BRCA1 and BRCA2 mutations [15]. About half of hereditary breast–ovarian cancer syndromes involve unknown genes.

GATA-3 directly controls the expression of estrogen receptor (ER) and other genes associated with epithelial differentiation, and the loss of GATA-3 leads to loss of

differentiation and poor prognosis due to cancer cell invasion and metastasis [16].

The two most commonly used screening methods, physical examination of the breasts by a healthcare provider and mammography, can offer an approximate likelihood that a lump is cancer, and may also detect some other lesions, such as a simple cyst [17]. When these examinations are inconclusive, a healthcare provider can remove a sample of the fluid in the lump for microscopic analysis (a procedure known as fine needle aspiration, or fine needle aspiration and cytology—FNAC) to help establish the diagnosis. A needle aspiration can be performed in a healthcare provider's office or clinic. A local anaesthetic may be used to numb the breast tissue to prevent pain during the procedure, but may not be necessary if the lump isn't beneath the skin. A finding of clear fluid makes the lump highly unlikely to be cancerous, but bloody fluid may be sent off for inspection under a microscope for cancerous cells. Together, physical examination of the breasts, mammography, and FNAC can be used to diagnose breast cancer with a good degree of accuracy.

Other options for biopsy include a core biopsy or vacuum-assisted breast biopsy [18], which are procedures in which a section of the breast lump is removed; or an excisional biopsy, in which the entire lump is removed. Very often the results of physical examination by a healthcare provider, mammography, and additional tests that may be performed in special circumstances (such as imaging by ultrasound or MRI) are sufficient to warrant excisional biopsy as the definitive diagnostic and primary treatment method.

Mammography and sonography are the standard imaging techniques for detection and evaluation of breast disease. Mammography is the most established screening modality. Especially in young women and women with dense breasts, sonography appears superior to mammography, and differentiation between solid tumours and cysts is easier. Sensitivity and specificity of sonography or mammography are higher if sonography and mammography are combined. Hence based on above findings the present study was planned to evaluate diagnostic accuracy of mammography and ultrasonography in breast cancer patients.

Methodology

The present study was planned in Department of Radio-Diagnosis, Narayan Medical College and Hospital, Sasaram, Bihar from Jan 2018 to July 2018. The 25 women's with breast lesions detected on clinical examination/self breast examination and referred for mammography and women in high risk groups (family history of breast cancer, previous history of breast cancer and disease like fibrocystic disease, excessive exposure to ionising radiation and history of endometrial, ovarian or colonic carcinoma.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: women's with breast lesions detected on clinical examination/ self-breast examination

Exclusion Criteria: Ulcerated and fungating breast growth, Pregnant women, moribund patients and proven cases of malignancy and male patients.

Results & Discussion

Breast cancer has a high prevalence in the community and places very high demands on resources. Historically, ongoing efforts are made to detect it as early as possible by using different clinical and imaging techniques. Self breast examination and routine clinical check-ups are clinical ways of detecting breast cancer early. However, due to the occult nature of most of the early breast cancers, imaging has a vital role to play.

Breast problem could be as simple as breast abscess to as ominous as cancer [19]. The breast lump besides creating anxiety may result in carcinoma and causes unbearable pain and deformity. Benign breast disease is so common that over half of the female population at some time in life seeks medical advice for breast problem, but effective evaluation and prompt diagnosis was needed to rule out malignancy. An early accurate diagnosis of breast disease has a favourable prognosis than that of late detection [20].

Ultrasonogram detects the lesion by the features of shape, margin, echogenicity, homogenicity, compressibility, posterior enhancement and calcifications. Ultrasonogram clearly differentiate carcinoma from benign disease with the features of irregular margin and shape, anechoic or mixed echogenicity and distorted architecture of surrounding breast parenchyma and evidence of microcalcification noted. The real advantage of USG was that solid and cystic masses could be differentiated well and young breasts with dense fibroglandular parenchyma could be imaged with ease.

Study done by Varela et al [21] was able to show the various impact of different approaches used, such that mammography was capable of detecting 94.5% of breast carcinomas; breast sonography detects 91% and palpation detects 87%. However, combinations of these approaches such as mammography and sonography or mammography and palpation detected 99% of carcinomas, while sonography and palpation detected 95% of carcinomas. Nevertheless, ultrasound is significantly more accurate in determining tumour size. [22] A study done by Sachin Prasad N and Dana Houserkova [23] in 2007 showed that mammography had a sensitivity of 82% for fibrocystic disease detected, 18 cases out of 22.

Table 1: Comparison of Mammography and USG

	Cytology	Mammography Alone	USG Alone	Combined
Fibrocystic disease	10	9	8	9
Infection	1	1	1	1
Fibroadenoma	2	1	1	2
Cyst	1	1	1	1
Carcinoma	5	3	2	5
Lipoma	1	1	1	1
Total	20	16	14	19

Table 2: Results of mammography diagnosing benign and malignant lesions

Mammography	FNAC proven-Carcinoma	FNAC proven - No carcinoma
Carcinoma	4	1
No carcinoma	1	14
Total	5	15

A study conducted by Karin Flobbe et al. in the Netherlands has estimated the prevalence of breast cancer to be 6.3%, which is consistent with the results of other studies [24]. Breast cancer detection via mammography has been recommended traditionally and the majority of women older than 40 years in the United States participate [25]. Recent research conducted on 210,000 women in Sweden has shown that in women aged 40-49 years, there was a significant 48% reduction in breast cancer mortality in those exposed to screening, whereas there was none in those unscreened [26].

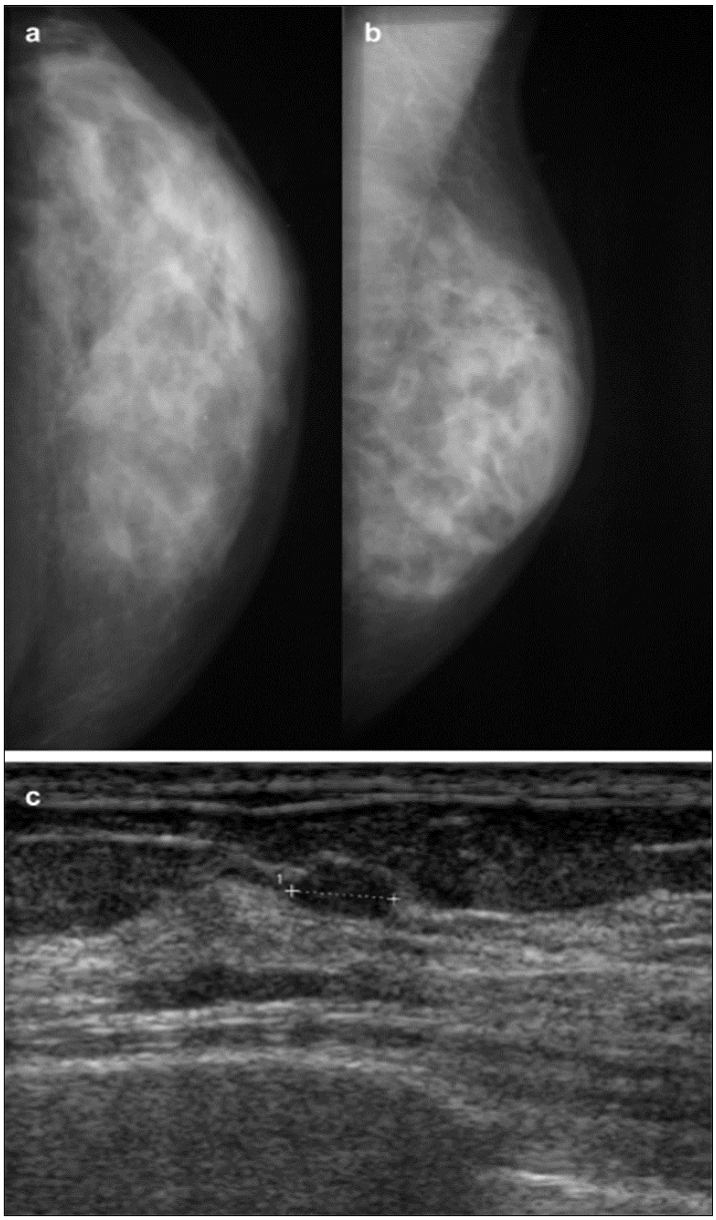

Fig 1: A & b: Mammograms and Figure C: Ultrasonography

Both screen-film mammography and digital mammography use x-rays to obtain images. With screen-film mammography, the image is captured on film; with digital mammography, the image is captured digitally [27]. Digital mammography is developed to address the limitations of film mammography and separates image acquisition and display, allowing the optimization of both [28].

In many recent studies, digital mammography was significantly better than conventional film mammography at detecting breast cancer in young women, premenopausal and perimenopausal women, and women with dense breasts [29]. The visibility of a subtle mass or cluster of micro calcifications present in the image can be increased if image contrast is adjusted [30]. Approximately 25-43% of non-palpable cancers are detected on mammography because of micro calcifications [31].

Bone et al [32] reported false-negative results in 11 out of 155 readings, with the majority being lobular cancers on histology. Lack of tumour-induced neovascularity may explain such findings. In particular, invasive lobular cancers infiltrate the normal tissue with columns of single cells, and receive adequate oxygenation without the requirement for

increased vascularization [33]. Buadu et al [34] found that lobular and mucinous carcinomas had a low microvessel density.

Kramer et al [35] reported that MR mammography yielded the highest sensitivity for detection of multicentricity as compared with mammography and sonography (89, 66 and 79%, respectively) in 38 patients. These findings are comparable with the present results, in which eight out of nine multicentric cancers were diagnosed correctly.

Mammogram can help the surgeon to determine whether a lesion is potentially malignant and also screen for occult disease in the surrounding tissue. Radio-opaque ball bearings mark the location of the mass and spot compression and magnification views can clarify the breast mass and determine its density [36]. If old films are available, they are compared with the new images. USG can effectively distinguish solid masses from cysts, which account for approximately 25 percent of breast lesions. When strict criteria for cyst diagnosis are met, USG has a sensitivity of 89 percent and a specificity of 78 percent in detecting abnormalities in symptomatic women. Recurrent or complex cysts may signal malignancy; therefore, further evaluation of these lesions is required. Although, USG is not considered a screening test, it is more sensitive than mammogram in detecting lesions in women with dense breast tissue [37]. It is useful in discriminating between benign and malignant solid masses and it is superior to mammogram in diagnosing clinically benign palpable masses [38].

Conclusion

Mammogram and ultrasonography are two important non-invasive investigations available for evaluating breast diseases. Mammogram is more efficient in diagnosing malignant diseases of the breast, whereas ultrasonography is more efficient in diagnosing benign breast diseases. The combinations of ultrasonography and mammogram will diagnose almost all diseases of the breast. In this study we confirm that ultrasonography when combined with mammography in detection of breast lesions has more specificity, sensitivity, and accuracy when compared to a single modality in detecting breast lesions.

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