Original article

Established Methods for Diagnosis of Breast Cancer in Tripoli, Libya

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Abstract

Background and aim*. Globally, breast cancer is one of the most frequent cancers among women. Methods for screening and diagnosis allow healthcare professionals to detect it early and provide personalized treatments that improve the outcomes and survival. It has been showed that various imaging techniques such as mammography, magnetic resonance imaging (MRI), positron-emission tomography (PET), Computed tomography (CT), and single-photon emission computed tomography (SPECT) could be used for diagnosis and monitoring patients with breast cancer in various stages.* ***Methods****. Seventy cases were diagnosed with breast cancer and were attending Breast Clinic at Tripoli University Hospital, Tripoli, Libya. The study revealed the most common tools used in Tripoli to diagnose breast cancer, stage of cancer and risk factors.* ***Results****. Most patients were within the age group ranged between 46 to 60 years (40%) and most cases with martial state married (77.1%). The first detection was at stage 2 in 37.1%. The most common risk factor was family history of breast cancer by 42.9% and unknown causes was 28.6%. Physical examination is the primary method for early breast cancer detection (92.9%), followed by ultrasound (60%) and mammogram (58.6%) while biopsy is the fourth tool by 35.7% and the fifth tool was MRI by 42.9%.* ***Conclusion****. The physical examination is the best diagnostic tool for early detection of breast cancer; however, have to also focus on other techniques with more sensitivity and specificity.*

Keywords*. Breast Cancer, Diagnosis, Imaging Tools, Stages, Tripoli, Libya.*

Introduction

In the world, breast cancer is the most-common cancer diagnosed among women and the first leading cause led to death from malignant tumors (1). Awareness of breast cancer, public attentiveness, and advancement in breast imaging has mode a positive impact on recognition and screening of breast cancer. Breast cancer remain a worldwide public health dilemma and is currently the most common tumor in the globe. It is life-threatening disease in females and the leading cause of mortality among women population. For the previous two decades, studies related to breast cancer have guided to astonishing advancement in our understanding of the breast cancer, result in further proficient treatments (2). It is a global issue now, but still it is diagnosed in their advanced stages due to the negligence of women regarding the self-inspection and clinical examination of the breast (2).

In fact, it is estimated that in 2025, 1.7 million new cases of breast cancer will be present in the developing world, and the huge discrepancy in survival chances will continue with most of the breast cancer deaths (70%) occurring in the developing world. Therefore, breast cancer has a tremendous public health significance and because primary prevention is still not available, efforts to promote early detection should be highlighted (3). Each year 2,3 million women are diagnosed with breast cancer(4).Early detection of breast cancer is the key for improving patients survival, as it gives insight regarding the most appropriate therapeutic strategy for each case (3).

Epidemiology

More than 2.3 million new cases of breast cancer each year, making it the most common cancer among adults. Worldwide, 95% of countries, breast cancer is the first or second leading cause of female cancer deaths. Yet, survival from breast cancer is widely inequitable between and within countries; approximately 80% of deaths from breast and cervical cancer occur in low- and middle-income countries (5). A study in 2021 estimated that 2.3 million cases and 685,000 deaths in 2020, and the cases might increasing to 4.4 million in 2070. Breast cancer in women accounted for approximately 24.5% of all cancer cases and 15.5% of cancer deaths which is ranked first for incidence and mortality in the majority of the world countries in 2020 (6).

In Libya, breast cancer is the first cancer which is about 1229 (16%) new cases diagnosed in 2020 according to Site of Cancer. According to the mortality rate breast cancer is the second cancer that leads to death with 459 cases (9.7%). the incidence rate by gender is 34.6% in females of the top 10 cancers and the mortality rate is 14.3% of the top 10 cancers.

Staging and grading of breast cancer

Pathologically, Stage of breast cancer is a measure of tumor size and spreading and is a prognostic term used to describe the predictable outcome of a cancer. However, grading of a breast cancer is a prognostic factor and is demonstrative of the "aggressive potential" of the tumor. American Joint Committee on Cancer (AJCC) staging system is mainly stands for anatomical staging, which used the TNM system by extent of the primary tumor (T), status of the regional lymph nodes (N), and metastasis status (M). Clinically, the T stage is based on the size and degree of loco-regional invasion by the primary tumor and is categorized from T1 to T4. The N stage is determined by the extent of nodal involvement including axillary, internal mammary, and ipsilateral supraclavicular lymph nodes. Distant metastases are evaluated to determine the M stage (7). Histologically, Tumor grade is an important prognostic factor independent of the tumor size and number of positive lymph nodes Tumor grade reflects tumor differentiation with worse prognosis observed in tumors with a high histologic grade or poor differentiation, than those with a low grade or well-differentiated (7). various ways to find out the stage and grade of breast cancer including, physical exams, biopsies, X-rays, bone scans and other images, and blood tests. a pathologist puts tissue samples from the breast and lymph nodes under the microscope to find out even more (7).

Tools using in diagnosis of breast cancer:

Currently, many methods are used to detect breast cancer in clinical practice include Breast Physical Examination (BPx), Mammography (including full-field digital mammography (FFDM) and DBT), Ultrasonography and MRI (Fig. 5). Positron Emission Tomography/Computed Tomography (PET/CT) is commonly used for diagnosis and staging. All these methods vary between one another regarding their utility, sensitivity and specificity (7).

Breast physical examination: breast self-examination (BSE) and breast physical examination (BPx) an important technique which affect identifying breast cancers at early stages (<3) suggesting they are effective screening tests with high availability and none invasive that can be useful at the community level. Refers to the inspection and palpation of the breast nipple and lymph-draining areas surrounding the armpit. This can be performed by (BSE) or by (BPx) (8-9).

Imaging diagnosis

The imaging techniques shows clearly the morphology and location of tumor and prove much clinical information. Yet, imaging techniques may cause harm to patients when using contrast agents and high-energy rays(10). These imaging techniques mainly include mammography (MG), ultrasonography (US), magnetic resonance imaging (MRI), positron emission computed tomography (PET), computed tomography (CT) and single-photon emission computed tomography (SPECT).

Mammography: the purpose of this method is to identify Journal Pre-proof malignant tumors before they are noticed. A mammogram consists of an X-ray examination of the breast in standard cranio-caudal and oblique views. However, the test can detect abnormal tissue but cannot prove that it is cancer so, can be misinterpreted, leading to unnecessary procedures and treatment. In addition, the sensitivity of mammograms is influenced by the age and density of breast tissue (41-42-43). By mammogram, the density of tissue layers limits

the detection of cancer tumors which could lead to additional tools to confirm detection, and also a biopsy of the breast tissue is recommended for histopathology analysis and molecular evaluation (11-12).

Ultrasonography: This is a diagnostic technique that uses high-frequency sound waves to produce images of internal mass structures, allowing the detection of abnormal tissues such as breast cancer. An ultrasound also might be used to determine if the lump/change is something benign (cyst, lymph node, benign tissue). Furthermore, is a guide for interventional procedures such as core biopsy, cyst aspiration, preoperative needle localization, and drainage. In ultrasonography, ionizing radiation and intravenous contrast are absent. Nevertheless, the ultrasonography detection rate for calcifications and specificity are low compared to mammography. In addition, a highly trained technician is required to carry out the test (13, 14-15).

Magnetic Resonance Imaging (MRI): uses primarily as an additional tool to breast screening with mammography or ultrasound. MRI is the most sensitive technique to detect breast implant ruptures when an appropriate protocol is performed. MRI uses strong magnetic fields and low-energy electromagnetic waves to produce detailed images of physiological processes of the body such as blood flow and nerve activity however needs Intravenous contrast (16-17).

Positron Emission Tomography/Computed Tomography PET/CT: refers to the technique, which combines PET and X-ray CT scanners to obtain images that identify the anatomic location of anomalous metabolic activity within the body. PET provides information of cancer physiology at the molecular level using radiotracers while CT produces pictures with the anatomic information therefore the patients should fast for several hours before PET/CT to optimize the study (18-19).

Biopsy: biopsy is a procedure to provide an accurate diagnosis as well as to determine the grading of cancer. After the detection of breast cancer abnormalities by imaging techniques, A biopsy is an invasive procedure where abnormal breast fluid or tissue is removed for cytological, histological and molecular analyzes. The test is recommended only in suspected cases of cancer based on the BI-RADS lexicon scale used by radiologists. Tumor biopsy is still the gold standard technique that confirms if a tumor is benign or malignant (20). There are three types of biopsies: 1) fine needle aspiration which is chosen to assess the liquid characteristics from cysts or abscess, 2) core needle biopsy which removes a small amount of the suspicious tissue, and 3) excisional biopsy that removes most or all of the abnormal tissue in conjunction with some healthy tissue (1). Different studies are focused on incidence and risk factors. Herein, this study aims to provide a consolidated focus on recent advancements in breast cancer diagnosis and therapy and also determine the most commonly established diagnostic tools used in breast cancer at Tripoli

Methods
Study type
All cases were diagnosed with breast cancer and were attending Breast Clinic at Tripoli University Hospital, Tripoli, Libya. The study determined the tools used in the diagnosis of breast cancer in Tripoli. The study is prospective to determine the most common diagnostic tools used in Tripoli, Libya. A total of 70 diagnostic cases performed from March to May 2023, Tripoli Hospitals were included in this study.

Data collection
Data was collected from patients who have been through breast cancer clinic, at Tripoli University Hospital, Tripoli, Libya. The study revealed the most common tools used in Tripoli to diagnose breast cancer. The questionnaire was divided into general information, risk factors, questions related to the tools used in diagnosis, and finally the stage of disease detection.

Statistical analysis
Data were entered and analyzed by Microsoft Excel software version 2019 and IBM SPSS STATISTICS. Answers frequency and percentage were used. Factor appearance proportion was tested using a sample t-test of Proportions to obtain probability $p < 0.05$.

Results

This study involved a group of 70 female patients diagnosed with breast cancer. The results revealed that the highest number of patients fell within the age range of 46 to 60 years, constituting 40% of the sampled population. Conversely, a very small number of women diagnosed with breast cancer were younger than 35 years by 2.9% of the study participants. Regarding marital status, most breast cancer patients were married, making up 77.1% of the total population (Table1).

Table 1. Shows the socio-demographic characteristics of the sampled breast cancer patients.

Characteristic	Frequency	Percentage (%)
Age		
15 – 25 years	2	2.9%
26 – 35 years	2	2.9%
36 – 45 years	22	31.4%
46 – 60 years	28	40%
More than 60 years	16	22.9%
Marital status		
Single	16	22.9%
Married	54	77.1%

Clinically, the first detection was at stage 2 in 37.1% of all cases. In contrast, a mere 4.3% of breast cancer patients identified their condition at stage 4. The primary risk factor observed in many patients was a genetic background for 42.9%. Unknown causes were 28.6%. In contrast, the least prevalent risk factor was exposure to radiation, affecting just 1.4% of the entire patient population (Table 2).

Table 2. Shows the clinical characteristics of the sampled breast cancer patients.

Characteristic	Frequency	Percentage (%)
Stage at which the first detection was made		
Stage I	23	32.9%
Stage II	26	37.1%
Stage III	18	25.7%
Stage IV	3	4.3%
Risk factors		
Genetic history	30	42.9%
Oral contraceptive	5	7.1%
Overweight or obese	8	11.4%
Exposure to radiation	1	1.4%
Increasing age	6	8.6%
Unknown	20	28.6%

The findings indicate that the primary tool employed in the identification of breast cancer was a physical examination, accounting for most cases at 92.9%. Notably, a physical examination was not utilized as a means of identification for the second, third, fourth, and fifth tools. Ultrasonography emerged as the predominant secondary method for detecting breast cancer, accounting for 60% of cases. Mammography followed behind as the second most frequently employed means of secondary identification. Furthermore, mammography surfaced as the most prevalent third method of identification, accounting for around 58.6% of

cases. In relation to the most used fourth means of identification, approximately 35.7% of instances were attributed to a biopsy. Lastly, the data indicated that about 42.9% of the samples utilized MRI as the primary fifth method for identifying breast cancer. A statistically significant distinction was found when comparing the tool number and its associated type in the detection of breast cancer (p= 0.001) (Table 3).

Table 3. Provides a summary of the various tools used in the identification of breast cancer and their corresponding number.

Tool number for disease identification	Type of tool used for disease identification						*P-value
	Physical examination	Mammo-graphy	Ultra-sonography	MRI	CT scan	Biopsy	
First tool	65 (92.9%)	1 (1.4%)	1 (1.4%)	0 (0%)	0 (0%)	3 (4.3%)	0.001
Second tool	0 (0%)	24 (34.3%)	42 (60%)	1 (1.4%)	0 (0%)	3 (4.3%)	
Third tool	0 (0%)	41 (58.6%)	10 (14.3%)	4 (5.7%)	4 (5.7%)	11 (15.7%)	
Fourth tool	0 (0%)	5 (7.1%)	8 (11.4%)	19 (27.1%)	13 (18.6%)	25 (35.7%)	
Fifth tool	0 (0%)	2 (2.9%)	1 (1.4%)	30 (42.9%)	15 (21.4%)	22 (31.4%)	

In relation to the connection between patients' age and initial diagnosis was made, it is clear that patients diagnosed at stage 1 were above the age of 60 and stage 2 was between 36 and 45 years. Moreover, 61.1% of breast cancer patients diagnosed at stage 3 were aged between 46 and 60 years. Finally, the majority of the study population diagnosed with breast cancer at stage 4 were 36 years or older. There was no statistically significant distinction observed between the age groups of the patients and the stage at which the disease was diagnosed (p= 0.458).The findings indicate that the majority of patients with a genetic history of breast cancer and those who used oral contraceptives were between the ages of 46 and 60. Both the age groups of 36 to 45 as well as 46 to 60 had a higher prevalence of obesity as a risk factor for breast cancer. All breast cancer patients exposed to radiation fell within the age group of 36 to 45. Older patients, specifically those over 60, were more likely to have increasing age as a risk factor. Additionally, 50% of the study participants with unknown risk factors were between the ages of 46 and 60. These results demonstrate a statistically significant correlation between risk factors and patients' age, with a p-value of 0.013 (Table 4).

Table 4. Clinical characteristics of the breast cancer patients.

Characteristic	Age of participants					*P-value
	15 – 25 years	26 – 35 years	36 – 45 years	46 – 60 years	More than 60 years	
Stage at which the first detection was made						
Stage I	1 (4.3%)	1 (4.3%)	6 (26.1%)	7 (30.4%)	8 (34.8%)	0.458
Stage II	0 (0%)	1 (3.8%)	12 (46.2%)	9 (34.6%)	4 (15.4%)	
Stage III	1 (5.6%)	0 (0%)	3 (16.7%)	11 (61.1%)	3 (16.7%)	
Stage IV	0 (0%)	0 (0%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	
Risk factors						0.013
Genetic history	0 (0%)	2 (6.7%)	7 (23.3%)	12 (40%)	9 (30%)	

Oral contraceptive	0 (0%)	0 (0%)	2 (40%)	3 (60%)	0 (0%)
Overweight or obese	1 (12.5%)	0 (0%)	3 (37.5%)	3 (37.5%)	1 (12.5%)
Exposure to radiation	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)
Increasing age	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	5 (83.3%)
Unknown	0 (0%)	0 (0%)	9 (45%)	10 (50%)	1 (5%)

Discussion

Diagnoses and treatment of breast cancer is still difficult as its behavior differs from one person to another. Various tools for screening and diagnosis are essential for detect cancer, and based on stage and future aggressiveness. Presently, breast cancer has become one of the health issues in human societies. Early diagnosis and detection of breast cancer play a vital role in its management and improve its survival rate. There are different methods for screening and diagnosing breast cancer including mammography, ultrasound, MRI, and biopsy. Each of these tools has different advantages and disadvantages. Although there are ways to improve these methods, they can be combined with different techniques to improve early detection of breast cancer (21).

Physical examination is a first diagnostic tool, however ultrasound screening significantly increases the detection of small-size cancers and early stage than Physical examination, which detects independently extremely few cancers(22). Study in France reported that the accuracy of clinical breast examination screening seemed to be low which did not support recommending regular Clinical breast examination(23).

As a routine examination, mammography recommended for women above 40 years of age (24). Study in China (2022) stated that sensitivity and accuracy of breast ultrasound was more than mammography in early diagnosis(95.7% vs. 78.9%,) while the specificity was significantly lower than that of mammography (42.9% vs. 62.3%) (25).

MRI is the most sensitive imaging modality for BC detection and is indicated for screening women at high risk for breast cancer and a non-invasive technique to measure the spatial stiffness of soft tissues, also used to evaluate cancer metastasis in patients with a known breast carcinoma. It is clear that MRI has benefits compared with mammography and ultrasound in screening and its role in cancer monitoring. (24,26).

Imaging tools are important to screen breast cancer though; diagnosis is influenced by percutaneous tissue biopsy which are includes morphological characteristics and the molecular pattern of the tumor. The main reason to perform a percutaneous biopsy is to avoid unnecessary surgery, associated morbidity, and costs for equivocal findings on imaging with final non-malignant histopathology. Moreover, axillary lymph node sampling adds information for cancer treatment(14). Bernathova M, et al. 2020, recommended that US and mammography-guided biopsies have sensitivity and specificity close to that of surgical biopsy with fewer adverse events and that non-imaging-guided free-hand procedures have lower sensitivity than image-guided methods (14).

Radiologists play a critical role in the detection and management of breast disease. Depending on the patient's history and lesion characteristics, the radiologist will take the best available biopsy. If a lesion is visible by Ultrasonography, it will be the preferred method for biopsy being most accessible, comfortable, and straightforward compared to other techniques. Some complications such as minor pain and bleeding are possible post-biopsy sequelae, nevertheless the risk of severe complications is actual low. Radiologic-pathologic association is important for an accurate and successful conclusion of the diagnostic procedure (14).

Conclusion

It is clear that breast cancer is still difficult to diagnose and treat as its behavior varies from one person to another. Our capacity to detect cancer, and define its stage is depended on different tools for screening and diagnosis. Age and cancer staging plays a critical role in choosing a diagnostic tool. The combination of more than one tool to diagnose breast cancer

is important to detect early diagnosis and improve cancer management especially since the tools are different in specificity and sensitivity. The findings of this study will help to detect perceived deficits in breast cancer and guide additional technique development therefore the combination of different techniques will facilitate a more comprehensive breast cancer valuation in the oncology field. Also health care professionals, technical experts and patients will lead to the development of better detection tools and methods for an improved screening and early diagnosis Furthermore, more research is needed to identify and evaluate the best tools for early diagnosis.

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