Early Detection of Recurrence and Prognosis of Breast Carcinoma in Young Women

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Abstract: Background: The goal of this study was to determine the outcome of treatment in young women with breast carcinoma and to identify imaging of choice for early detection of recurrence. *Methods:* We have 30 patients ≤ 30 years who diagnosed as invasive breast carcinoma in the period from September 2007 to September 2009 and follow up for 3 years. In this prospective study we obtain the data of patients from the medical records including history taking clinical examinant local and general and routine and specific investigation including laboratory and radiological also metastatic work up. Other group of patients, more than 30 years age diagnosed as breast carcinoma used as a control group (n=30). *Results:* We have two groups of patients studying group ≤30 years, control group > 30 years each group is 30 in number of cases in the studying group. The following data were obtained: 10%, 46.66%, 33.33% and 10% for stages I, II, III and IV respectively.Mastectomy was done in 27 case (modified radical mastectomy) breast conserving surgery in three cases (one case stage I, two cases stage II).*Conclusion:* Women who are diagnosed as breast carcinoma at ≤30 years appear to have a poorer prognosis in comparisons with the group who > 30 years. Kinetic MRI and MRS, are the imaging of choice for detection of recurrence.

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Keywords: Breast carcinoma, Young women, Prognosis, American Joint Committee on Cancer, Mastectomy, Breast conserving surgery. MRI.

1. Introduction

Breast carcinoma is the most common type of cancer in women in Egypt & Arab countries and is the second leading cause of cancer death in women in United States. Most breast carcinoma occurs in postmenopausal women [(1)]. Women age ≤ 39 years account for approximately 5.9% of all patients with breast carcinoma In spite of small number of young women diagnosed as breast carcinoma it has bad effects on these patients, their families and societies[(3)].

Some surgeons recommend more aggressive treatment approaches for young women who have carcinoma of the breast. However, others have been unable to confirm this finding. Therefore it is important for clinician and patients to resolve, clarity and understand this controversy[(2,5)].

• Types of local recurrence:
o True recurrence: Recurrence at site of primary tumor, within area that received XRT boost, usually in cases with close or positive margins, most frequently seen within first 5 yrs post treatment.
o Marginal miss: Recurrence near site of primary tumor, adjacent to area of boost, usually in first 5 yrs
o Elsewhere recurrence: Tumor in ipsilateral breast away from original tumor, presumed to represent a new primary, risk same as for contralateral breast.

Lactatinb c:
• General path comments: Similar to non-pregnancy-related carcinoma
o BRCA-1& -2 gene carriers more prone
• High levels of estrogen may accelerate malignancy
o Family history of breast cancer more common
o - 3% of all breast carcinomas
o Most common malignancy in pregnancy
• 1:3,000-10,000 pregnancies
o Incidence of inflammatory carcinoma similar to non-pregnancy-related carcinoma
• Histologically similar to non-pregnancy-related carcinoma, but higher incidence of some findings

2. Patients and Methods

We have 30 patients ≤ 30 years who diagnosed as invasive breast carcinoma in the period between september; 2007 and september 2009 & follow up for 3 years at Al-Azhar university hospitals (Al-Hussein & Sayed Galal) and Al-Amin hospital (Taif- KSA). Other group of patients (more than 30 years old) diagnosed as breast carcinoma used as a control group.

In this prospective studies we obtain the data of patients from the medical records including history taking, clinical examinant "local and general" and routine and specific investigation "laboratory and radiological" also metastatic work up.

The diagnosis of recurrence depends on imaging criteria, nuclear medicine and biopsy:

All diagnostic modalities were used, Mammography, US, MRI, MRS, we try to measure sensitivity and specificity of these diagnostic modalities.

Examination protocol and technique:

Mammography:

o Computed radiography FFDM (CR-FFDM): Storage

phosphor plate captures X-ray photons; laser plate scanner extracts digital image
• Craniocaudal view (CC)
• Mediolateral oblique (MLO)
• Mediolateral view (ML)
• Lateromedial view (LM)
• lnframammary fold (lMF)
Breast Imaging Reporting and Data System (BI-RADS) was applied
US: High frequency transducers were used in the range of 10 MHz. (Linear phased array transducer) (GE logic 9). The depth of focus is usually set at 3 cm or less.
Imaging Protocols
• High frequency linear array transducer with center of frequency 10 MHz preferred
o Color, power Doppler helpful
• Scan planes
o Breast ducts are arranged radially from nipple
• Lesions tend to grow along duct system
o Scan in radial and antiradial (orthogonal to radial) planes for lesions
• Maximal diameters in perpendicular planes
o Survey scanning: Transverse and sagittal more efficient at covering entire breast
o Images labeled with scan plane, clock face, distance from nipple in cm
• Use transducer width (e.g. 38 or 50 mm) as measuring guide
• Positioning: Area of interest is as thin as possible
o Supine for medial breast
o Oblique with arm above head for lateral breast
o Patient can elevate breast for inferior lesions
• Field of view to reach chest wall but not beyond
• Color Doppler
o Vocal fremitus: Tissues vibrate when patient hums; movement -+ "color"
• Mass vibrates < normal tissue -+ defect in color-filled background
o Internal vascularity in solid masses
• May help with identification of papilloma in distended duct
• Must be familiar with US artifacts to avoid interpretation pitfalls
MRI study: was performed using 1.5-T whole body MRI and spectroscopic system (GE and Philips medical systems using a bilateral standard phased array breast coil.

Imaging Protocols
o Dedicated phased array breast coil, ~ 1.5T
o Simultaneous bilateral acquisition, prone position
o Axial or sagittal plane
o T1WI without fat suppression
• Fat (e.g., fat necrosis, hila of lymph nodes) hyperintense
• Acute blood hyperintense
o T2WI with fat suppression or STIR
• Fluid (e.g., cysts, seromas) hyperintense
• Myxoid fibroadenomas, mucinous carcinomas canappear hyperintense
o 3D spoiled gradient echo volume acquisition (T1WI)with fat suppression
• Resolution 1 mm x 1 mm x not more than 3 mmslice thickness
• Pre-contrast: Establish appropriate field of view
• Inject 0.1 mmol/kg Gd-contrast IV, ideally with power injector
• Image both breasts within 2 minutes of injection
• Image both breasts ~ 5 minutes post-injection
o Post-processing of 3D data set
• Subtract pre-contrast from post-contrast images ateach time point
• 3D MIP images from subtraction dataset
• Optional: Computer-assisted parametric mapping
(CAD) of kinetics
• CAD includes thresholding: ~ 50-60% enhancement in first 2 minutes
• CAD color coding of 3-4 pixel areas of persistent, plateau, and washout kinetics
1H MRS Protocol and analysis:
Using localized single voxel technique with the point – resolved spectroscopic sequence (PRESS). The voxel was placed on the post injection subtraction images. The voxel size ranged from 4.2 to 8 cm3. It was curefully positioned to cover the enhanced lesion without contamination with the surrounding tissues. The water suppression was performed by using a PRESS with 3 pulse chemical shift selective CHESS. The fat signal was independently attenuated by using frequency selective lipid suppression technique. The PRESS acquisition .sequence parameters were :TR/TE=1200/270; flip angle, 90; 512 measurements. The sequence acquisition time was 12 min. This relatively long TE (270 ms) was chosen to increase the visibility of the Cho resonance because of the longer T2 of Cho in comparison with that of lipids. The absolute Cho levels were quantified by using a Gaussian line-shape fitting model and the unsuppressed water signal was used as an internal reference. (15)
Recurrent B C, radiological findings (16):
Mammographic Findings
• 35-50% of recurrences mammographically detected after BCT
o DClS: New suspicious Ca++, esp. fine linear, linear distribution, pleomorphic
o Invasive carcinoma: Ill-defined, increased density/mass or spiculated mass, more distortion
o May be stable for months or years before enlarging

Ultrasonographic Findings
• Grayscale Ultrasound
o Benign scar commonly causes posterior shadowing
• Mass-like; extends to skin scar
o Hematoma/seroma common 6-12+ months post-op
• Resolves sooner if no XRT or intra-operative brachytherapy
o Recurrent invasive carcinoma: Irregular hypoechoic mass, often near scar
MR Findings
• TlWI
o Mass or distortion, hypointense to parenchyma
o Fat necrosis, hematoma hyperintense centrally
• T2WI FS: Mass or distortion, hypointense to parenchyma
• Tl C+ FS
o Benign scar enhances up to 6 months post-BCS, up to 18 months post-BCT; can be longer
• Thin, smooth rim around seroma
• Fat necrosis can enhance even years later
o Parenchymal enhancement common post-XRT
o Enhancing irregular mass suspicious for invasive carcinoma
o Linear enhancement suspicious for DClS
Kinetics
• Sample and report ROI's of most rapidly enhancing ± most suspicious areas in lesion
• Initial phase: Change in SI within first 2 minutes of injection (before curve changes)
o Suggested thresholds are listed in CAD programs vary
o Slow: < 60% increase in SI within 2 minutes
o Medium: 60-100% increase in SI within 2 minutes
o Rapid: > 100% increase in SI within 2 minutes
• Delayed phase: Enhancement pattern
o Persistent (Type I): Progressive, continued increase in signal over time i 6% malignant
o Plateau (Type II): SI does not change over time after initial rise in flat (± lO%)i 64% malignant
o Washout (Type III): SI decreases after peaking; 87% malignant
• Normal lymph nodes often show washout kineticsI

3. Results:
Tables from (1- 5) and figs from (1-7):

Table (1): Patients' characters

Characteristics	Study patient N(%)	Control patient N(%)
Age		
14-19	5 (16.66)	-
20-24	8(26.66)	-
25-30	17(56.66)	-
31-40	-	6(20)
41-50	-	10(33.33)
51-60	6-	14(46.66)
Race		
White	20(66.66)	25(83.33)
Black	10(3.33)	5(16.66)
Histology		
Ductal carcinoma	25(83.33)	27(90)
Lobular carcinoma	5(16.66)	3(10)
Receptor status		
ER+PR-	2(6.66)	-
ER-PR+	3(10)	-
ER+PR+	10(33.33)	-
ER-PR-	10(33.33)	-
Unknown	9(30)	-

ER: estrogen receptor. PR: progesterone receptor, +: positive, -: negative

Table (2): In Study group ≤30 years disease stage at presentation and treatment by stage.

Treatment	Stage: No. of patients %			
	I	II	III	IV
Surgery	3(10%)	14(46.66%)	10(33.33%)	3(10%)
Mastectomy	2	12	10	3
BCS	1	2	-	-
Radiation	3	14	10	Not applicable
Neoadjuvant or adjuvant chemotherapy	1	10	8	Not applicable

BCS: Breast consening surgery
In patients above 30 years we have
30 patients 15 cases stage I
10 cases stages II-III
5 cases stage IV
This group used as control group

Table (3): Three years recurrence free and overall survival rates by stage.

Rate	Stage (%)			
	I	II	III	IV
RFS	46%	49%	32%	-
OS	87%	60%	42%	16%

RFS: Recurrence free survival
OS: Overall survival

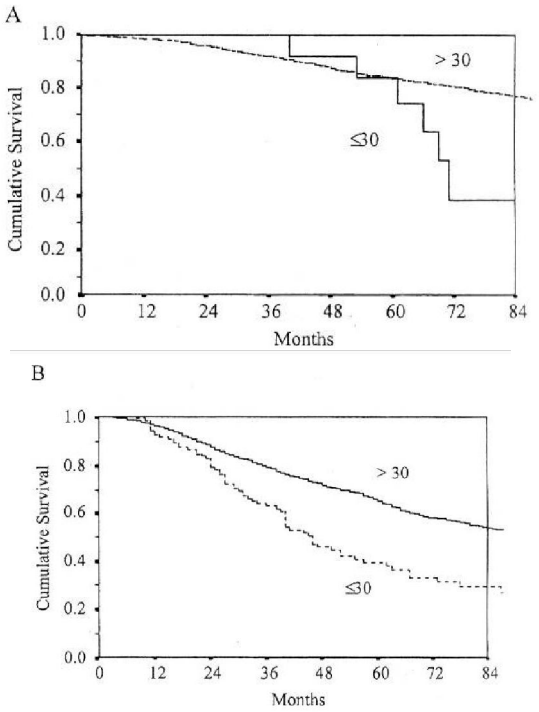
Table (4): Three year overall survival rate in women age ≤30 years and > 30 years.

Age (years)	Stage (AJCC)		
	I (local)	II, III (regional)	IV (distal nt)
≤30 No. of patients	2	11	-
OS rate	66.66%	50%	-
> 30 No. of patients	12	7	2
OS rate	80%	70%	40

AJCC: American Joint Committee on Cancer
OS: Overall Survival

Table (5): Statistical analysis of the diagnostic modalities in Study group ≤30 years

Modality	Results			
	True +ve	False +ve	True –ve	False -ve
Mammography	11(+ve predictive value=50%)	6	2	11
US	17(+ve predictive value=77.27%)	4	4	5
MRI&MRS	21(+ve predictive value=95.4%)	1	7	1



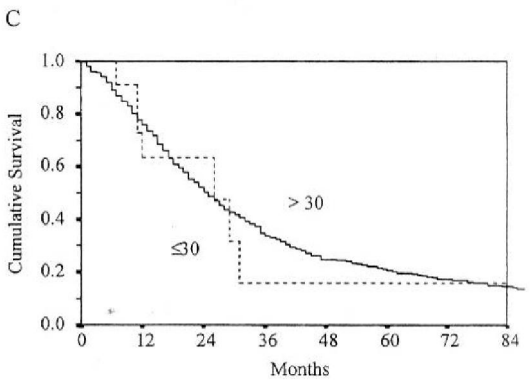
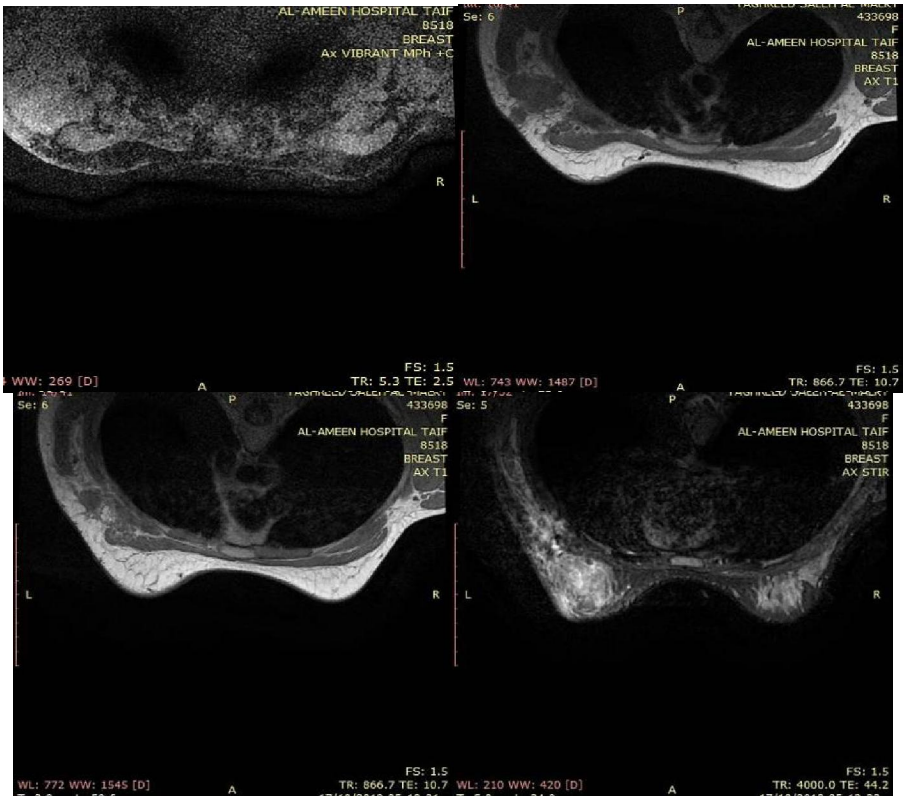


Fig. 1: Overall survival rate in women age ≤ 30 years and age > 30 years. The SEER staging system was used for women age > 30 years, and the American Joint committee on Cancer Staging system was used for women age ≤ 30 years. A) women with stage I local diseases. (B) women with stage II and III regional disease. (C) woman with stage IV distal disease.



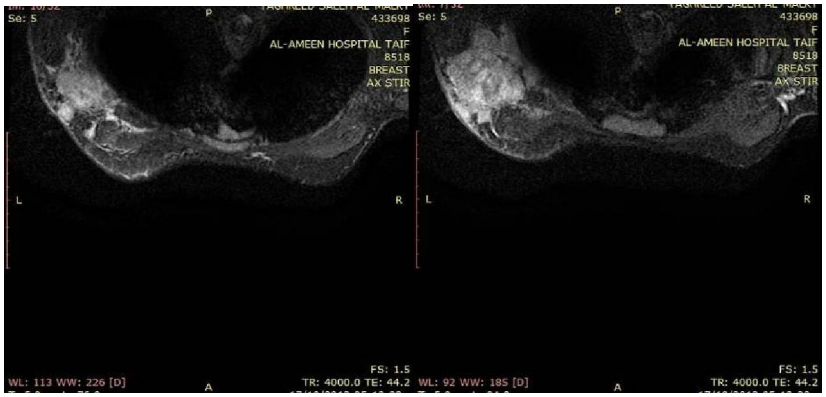


Fig2: Axial, T1, Stair, T1FS +C : 3 O;Clock ill defined soft tissue distortion, irregular enhancing pattern with axillary enhancing LN

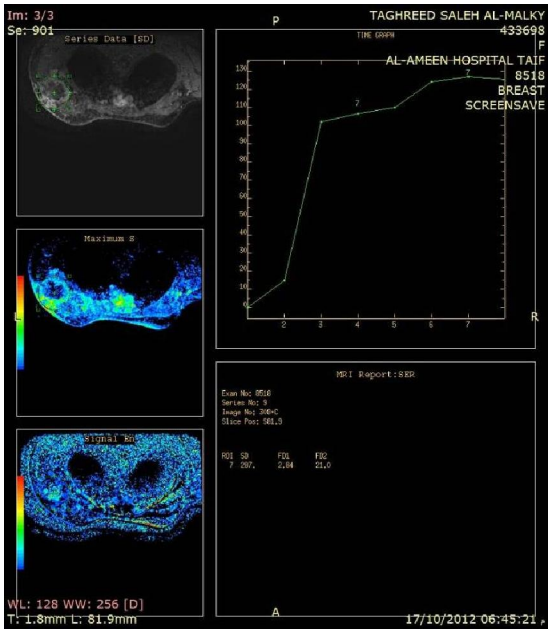
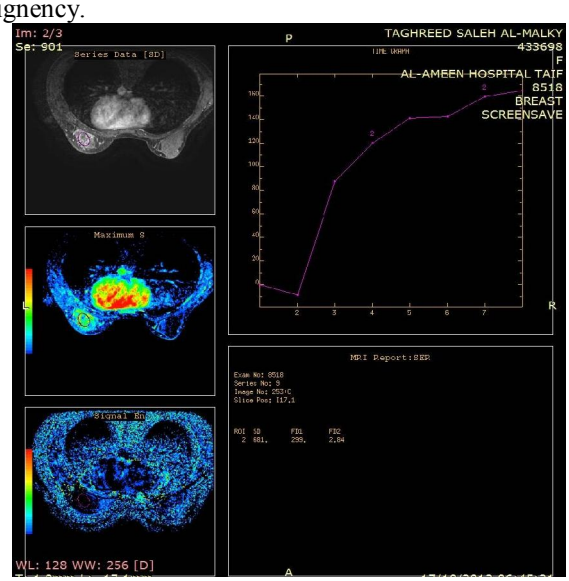


Fig3: Kinetic curve: initial change in signal intensity (first 2 minutes of injection)=100 %, Delayed phase: platue curve (type II)=64%malignency.



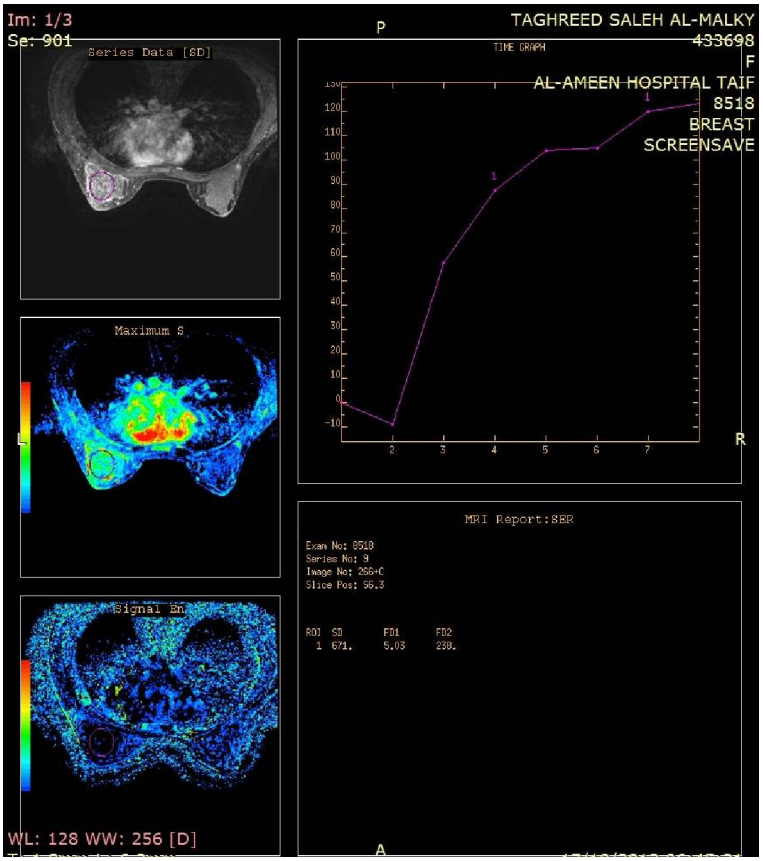


Fig4: Surrounding soft tissue revealed medium initial phase and type I delayed phase=6% malignancy

MRS curve revealed +ve choline with high peak at 3.2 ppm:(Fig5)

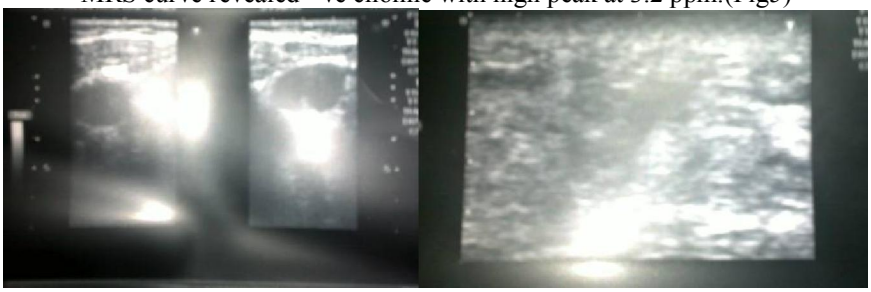


Fig6: US:focal solid lesion at 3 O'Clock=23x12 mm, speculated margin, architextural distortion, scar tissue is noted-the right images show enlarged axillary LN of metastasis (same case of MRI).

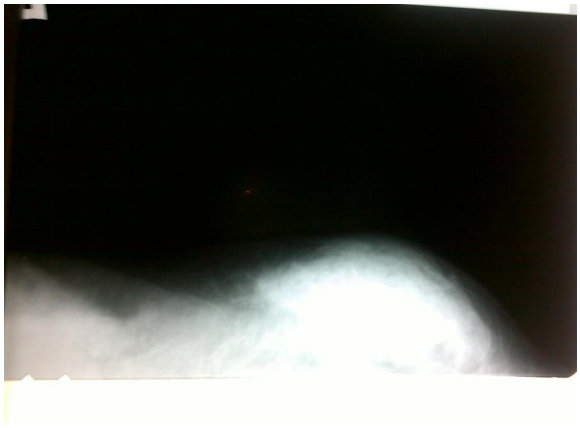


Fig7: Mammography: revealed dense ill defined lesion, speculated margin at the upper lateral quadrant+ axillary LN enlargement.

4. Discussion

This study documents the natural history of a young woman with breast carcinoma who received treatment at a single unit (Oncology Unit). The results support previous observation that women who have diagnosis of breast carcinoma at a young age have a poorer prognosis compared with older women.

Criticisms of previous reports included insufficient sample size. Study period is much longer for many years during which treatment damaged, and lack of valid control population [4,7].

So to correct some of these limitations large number of cases are used in a single institution, relatively short period, control group came from the same institution and the same period of time [4,6].

Explanation of more cases of advanced breast carcinoma in young women may be due to lack of valid screening mechanisms or awareness, decreased efficacy of mammography, breast carcinoma in young women is more aggressive some studies have shown that breast carcinoma in young women is more aggressive biologically[9], also carcinoma of the breast in young women is poorly differentiated, tumor is less likely to be ER positive or PR positive, more likely to have P53 protein expression, HER_2/ new over expression is detected in about 26% of patients with breast carcinoma, worse histological grading, high rate of proliferation, poor prognosis[10].

Kroman et al. reported that young women with low risk breast carcinoma who did not receive adjuvant treatment have a significantly increased risk of death from breast carcinoma [8].

Fowble et al. reported that young women with early stage of breast carcinoma with a negative [9].

Lymph node had relatively worse prognosis our observation in our study support the importance of adjuvant chemotherapy for young women in stage I. despite receiving appropriate treatment young women ≤30 years with stage II or III had a worse prognosis of compared with older patients in the institution or centre.

Young women with breast carcinoma has poor prognosis due to physician or patient delay in diagnosis young women with breast carcinoma in spite of undergoing multimodality treatment stressed that the need for better understanding the biology of breast carcinoma in young women and for developing new treatment strategies for this group of patients.

In our study, mammography revealed relative lows sensitivity and specificity for detection of cancer recurrence, its accuracy=43.3%

It is likely related to post-operative fibrosis and deformity.

US revealed relative higher sensitivity and specificity in detecting tumor recurrence in comparison with mammography, its accuracy=70%

Boetes et al,(11) reported that US has a limited role in excluding early malignancy.

Our study confirmed the results of (12-13-14) who said that MRI & MRS revealed high sensitivity and specificity in detection of cancer recurrence, its accuracy=93.3%.

Our recommendation: as we know breast carcinoma in young women have poor prognosis compared with older ones, the physician should oriented by this subject , select the imaging of choice for early detection of recurrence and should encourages for health education for all population sectors and all patients should participate or share to obtain the optimum and good therapy.

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