

ASSESSMENT OF NEO-ADJUVANT THERAPY IN CORRELATION WITH THE PREDICTIVE ROLE OF KI67 INDEX IN CASES OF LOCALLY ADVANCED BREAST CANCER

*Manar Shaaban Saleh**; *Reda Abd Eltawab Khalil***; *Ashraf Abd El Moghny Mostafa***; *Hany Abd Elaziz****; *Lobna Shash*****; and *Yasser Mohammed Abd El Samea***

ABSTRACT:

* General Surgery Department
Ismailia, Hospital
General Surgery, * Nuclear
Medicine and ****Pathology
Departments
Faculty of Medicine, Ain Shams
University , Cairo, Egypt.

Corresponding author

Manar Shaaban Saleh
Mobile: +201009933700
E.mail:
beauty_n1@hotmail.com

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Background: Neoadjuvant therapy refers to the administration of systemic therapy, either chemotherapy or endocrine therapy, prior to definitive breast surgery. Patients who derive clinical benefit from neoadjuvant chemotherapy (NACT) include patients with high-risk breast tumors, large breast tumors, and locally advanced tumors, including those initially ineligible for surgery. The goals of NACT include rendering inoperable tumors resectable, surgical down staging for patients who prefer breast conservation, and de-escalating axillary surgery in those with clinically positive nodes.

Aim of the Study: To evaluate the response rate to neoadjuvant chemotherapy or hormonal therapy in cases of early breast cancer (T1, T2-N0, N1-M0) according to the TNM staging and to find the predictive value of the reduction of the prognostic value Ki-67 for the response to the neo-adjuvant treatment.

Patients and Methods: This prospective study was conducted at tertiary care hospital at the breast surgery unit and clinical oncology departments, Ain Shams University Hospitals from 2015 till 2017 and performed on a total of 60 female patients with newly diagnosed early breast cancer patients according to TNM staging system.

Results: During the follow-up of the patients, the current study results revealed that Ki-67 was significantly decreased with significantly decreased tumor size at follow up among the studied cases. Baseline and follow up Ki-67 were lowest in complete response, followed by partial response, then stable disease and highest in progressive response, the differences statistically were significant. As a result, Ki-67 statistically had significant moderate diagnostic performance in predicting clinical responses, was highest in predicting progressive response.

Conclusion: Ki-67 is a valuable marker, as it has prognostic and predictive abilities after neoadjuvant chemotherapy. Ki-67 expression may be considered a valuable potential biomarker and add a prognostic information to that obtained from classical prognostic factors such as tumor size.

Keywords: Breast Cancer; Ki67; Neo-adjuvant Therapy

INTRODUCTION:

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females, accounting for 23%

(1.38 million) of the total new cancer cases and 14% (458,400) of the total cancer deaths in 2010. About half the breast cancer cases and 60% of the deaths were estimated to

occur in economically developing countries. The crude incidence of breast cancer in Europe was 109.8/100.000 women per year and it is responsible for 38.4 out of 100.000 deaths per women annually⁽¹⁾.

In Egypt, breast cancer is the most common cancer in females, it represented 37.6% of all cancer cases in Gharbia cancer registry 1999 and 37.5% of all cancer cases presented to the national cancer institute between the year 2002 and 2007⁽²⁾.

Comparative clinic-pathological studies have shown that Egyptian breast cancer is particularly aggressive with large tumor size, more poorly differentiated histology and higher incidence of nodal metastasis⁽³⁾.

Neoadjuvant chemotherapy is the standard treatment modality in locally advanced breast cancer and inflammatory breast cancer, and accepted as an alternate modality in operable breast cancer⁽⁴⁾.

The term neoadjuvant chemotherapy (NACT) is used to describe chemotherapy given before loco-regional therapy. Despite the prefix 'neo' from Greek meaning 'new' with the adjective 'adjuvant' from Latin meaning 'assistant', such treatment is not new; it was shown to be effective therapy in a well documented study carried out by von Essen et al., more than three decades ago. It was originally used in locally advanced inoperable disease in order to achieve surgical resection. It was then extended to operable breast cancer with a view to down-staging tumors to facilitate breast-conserving surgery. Increasingly, it is being considered as a treatment for earlier-stage disease⁽⁵⁾.

Neoadjuvant chemotherapy and hormonal treatment could allow the examination of molecular and genetic profiles of individual tumors to predict the response of a particular chemotherapy regimen and hormonal treatment, thereby eventually providing the promise of individualized therapy for women with breast cancer⁽⁶⁾.

Advantages of primary systemic therapy or the neoadjuvant chemotherapy and hormonal treatment include: decreasing tumor size, consequently, allowing the surgeon to preserve the breast, in vivo testing to tumor response to specific drug treatment and future potential response to further treatment and finally, it may be informative about the biology of the carcinoma under treatment. Many studies assessed the efficacy of neoadjuvant systemic therapy and comparing it to adjuvant therapy⁽⁷⁾.

The rationale of preoperative or neoadjuvant chemotherapy and hormonal treatment in patients with operable breast cancer originated from experimental and clinical observations as well as theoretical hypotheses on tumor cell growth and dissemination which justified the use of neoadjuvant chemotherapy and hormonal treatment for the purpose of early systemic control without affecting progression or survival of the patients⁽⁸⁾.

Further clinical justification for the use of neoadjuvant chemotherapy was provided by the demonstration of long term (up to 20 years) equivalent survival between breast conserving surgery with radiotherapy and mastectomy in patients with early breast cancer⁽⁹⁾.

As mentioned above, the potential for increasing the rates of breast-conserving surgery in patients with operable breast cancer is probably the most important clinical advantage of neoadjuvant versus adjuvant chemotherapy. Based on this development, neoadjuvant chemotherapy could be employed irrespective of nodal status with the intent to convert patients needing mastectomy to candidates for breast-conserving surgery. However, besides that, the use of neoadjuvant chemotherapy has the potential to improve the cosmetic result by decreasing the amount of breast tissue that needs to be removed at the time of lumpectomy⁽¹⁰⁾.

Patients with no axillary metastases in the post-chemotherapy mastectomy specimen had the best outcome, with nearly 80% surviving at 5 years; in contrast, fewer than 10 % of patients with 10 or more positive nodes survived 5 years. Not surprisingly, patients with an intermediate number of residual metastatic nodes had an intermediate survival rate and the axillary nodal status retains its prognostic value, as demonstrated by van Nijnatten et al. in a study of 136 LABC patients undergoing modified radical mastectomy after induction chemotherapy⁽¹¹⁾.

Although induction chemotherapy has dramatically improved the operability of LABC, local failure rates of 20% to 30% have been reported for patients managed with systemic therapy and surgery alone⁽¹²⁾.

Neoadjuvant protocols were introduced for LABC group of patients first to downstage them and then these neoadjuvant protocols were used in the early stages also to improve the surgical options and increase the organ preservation surgeries⁽¹³⁾.

Pathological complete response (pCR) during the neoadjuvant protocols was significantly improving the progression free survival (PFS) and overall survival (OS) of these patients⁽¹⁴⁾.

Also dose dense regimens were used with marginal benefit on progression and survival with minimal improvement in the pathological complete response (pCR)⁽¹⁵⁾.

Also neoadjuvant studies tried to evaluate different prognostic markers to know their impact on the response and survival. Proliferation index was evaluated as prognostic marker; Ki-67 was used as a proliferation index in several studies⁽¹⁶⁾.

AIM OF THE WORK:

The aim of this study is to assess the predictive value of the reduction of the prognostic value Ki-67 in patients receiving neoadjuvant chemotherapy or hormonal

therapy in cases of early breast cancer (T1, T2, -N0, N1-M0) according to TNM staging.

PATIENTS AND METHODS:

This study was conducted at the breast surgery unit and clinical oncology departments, Ain Shams University Hospitals during the period from 2015 to 2017. During this study, 85 patients were assessed for eligibility and 60 patients were included in the study. Of all eligible patients, 18 patients were excluded from the study based on the inclusion criteria and 7 patients refused to participate in of the study. Ultimately, the analysis was based on the data of 60 female patients with newly diagnosed early breast cancer patients according to TNM staging system.

Patients were enrolled in this according to the following inclusion criteria: Females with pathologically proved breast cancer and their Ki 67 index ≥ 20 %, tumor size less than 5cm (T1, T2), axillary lymphnode states is (N0, N1), eastern Cooperative Oncology Group (ECOG) performance status of zero to two⁽¹⁷⁾, adequate hematological, renal and hepatic functions, left ventricular ejection fraction (LVEF) within the normal range ($\geq 50\%$), and patients were required to have measurable disease according to the Response Evaluation Criteria in Solid Tumors (RECIST)⁽¹⁸⁾. While pregnant or lactating females, inflammatory breast cancer patients, presence of distant metastasis, patients received chemo, radio or hormonal therapy before, previous cancer within the last 5 years or a second primary malignancy, patients with serious infections or severe illness that prevent the use of chemotherapy were excluded from the study.

Study Design:

I. Pretreatment Evaluation:

All patients were evaluated by history taking and full clinical examination including assessment performance status of the patient

based on the ECOG performance status scale⁽¹⁷⁾.

Local examination of the breast and axilla with assessment of the breast mass size and lymph node staging was done according to TNM staging. Bilateral breast sonomammography was performed for TNM staging on the basis of clinical and radiological findings. Tru-cut biopsy from the tumor was taken and processed into paraffin blocks which were used for preparation of Haematoxylin and Eosin (H & E) sections for assessment of tumor type and histologic grade and also for immunohistochemical analysis for ER, PgR and Her-2neu and proliferation index Ki-67. Laboratory investigation was done in the form of complete blood picture, liver and kidney function tests. Radiological examination in the form of CT scan of the chest, abdomen and pelvis and bone scan were requested to exclude distant metastasis. Echo-cardiography was done for the patient prior to the start of the neo-adjuvant treatment.

II. Treatment Strategy:

This study was a phase II trial of using neo-adjuvant chemotherapy or hormonal therapy if required in treating operable and early detected breast cancer patients. Complete blood cell count was obtained before each chemotherapy treatment. Another tru-cut biopsy was taken on the 15th to 20th day after the 1st cycle of chemotherapy and after 2 months (the 60th day) after starting the hormonal treatment to re-measure the Ki 67 index, if the index decreased (about 50% from the initial value of the Ki 67) the rest of the treatment were proceeded while if it doesn't decreased we had directly proceed to definitive surgical strategy according to the case.

Surgical strategy:

When the decision of surgical treatment is taken we assessed the cases individually if the initial tumor mass size is < 2 cm, ultrasound guided metallic clip was applied

into the site of the original mass to help in making complete excision of the tumor area after finishing the neo-adjuvant treatment because it could get complete response (CR) after the 1st cycle. While if the initial tumor mass size is ≥ 2 cm and after the 1st cycle their Ki 67 index become < 30% so this patient may developed (CR), ultrasound guided metallic clip was applied into the site of the original mass after the 1st cycle. The conservative breast surgery and oncoplastic breast-conserving reconstruction surgery were the ideal surgical modalities to our patients with complete response (CR) and partial response (PR) cases after finishing their neoadjuvant treatment, modified radical mastectomy (MRM) were another surgical alternative for some certain cases. The surgical specimen was processed and examined to assess the pathological response in the primary tumor and axillary lymph nodes and for immuno-histochemical analysis of the proliferation index Ki-67 by using MIB-1 antibody. After surgery the patients received radiotherapy according to the clinic-pathological criteria. Once indicated patients received conventional radiation therapy 2 Gy\fraction, 5 factions\week, 50 Gy for the chest wall for patients who underwent modified radical mastectomy and the same dose to the whole breast for patients who underwent conservative surgery with boosting by 10 Gy on the tumor cavity. Hormone responsive patients received hormonal treatment for 5 years according to their menopausal status.

III. Evaluation of response:

All patients were evaluated for response every one cycle chemotherapy and 2 months hormonal therapy by clinical examination and Bilateral sono-mammography and\or bilateral breasts MRI in some certain cases; before the surgery or at any time of the treatment to document progression of the tumor.

A. Clinical evaluation of response:

Evaluation of response was done according to the RECIST criteria of response by *Therasse et al.*⁽¹⁸⁾:**Complete response**

(CR) means the disappearance of all target lesions. **Partial response (PR)** means at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum longest diameter. **Progressive disease (PD)** means at least a 20% increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum longest diameter recorded since the treatment started or the appearance of one or more new lesions. **Stable disease (SD)** means neither sufficient shrinkage as for partial response nor sufficient increase as for progressive disease, taking as reference the smallest sum longest diameter since the treatment started. **Duration of response:** (Complete response, Partial response and stable disease) were calculated from the date of first assessment of response to the date of first progression.

B. Pathological response:

Pathological evaluation of response was done based on Sataloff criteria of pathological response Where Class A referred to complete or quasi-complete response, Class B referred to partial response, Class C referred to minor response and Class D referred to no response (19).

Table (1): Demographic characteristics of the studied cases

Characteristics		Mean ± SD	Range
Age (years)		48.4±5.6	39.0–60.0
		N	%
Hormone status	Positive	29	48.3
	Negative	31	51.7

Total=60

Table (1) shows that: **Demographic characteristics** among the studied cases.

The baseline (initial measurement before receiving any neoadjuvant treatment) for Ki 67 % among the studied

Table (2):Ki-67 (%) among the studied cases

Time	Mean±SD	Range	^p-value
Baseline	55.7±13.8	28.6–83	<0.001*
Follow up	40.3±21.9	9-85	
Change percent	-32.7±21.0	-67.8–2.4	

Total=60. Change = After – before, negative values indicate reduction. ^Paired t-test. *Significant.

V. Follow up of the patients:

After finishing the treatment all the patients were scheduled for follow up as following: Clinical examination and history taking every 3 months. Annual sonomammography. CT scan of the chest and/or pelvi-abdomen were performed only if clinically indicated or there are symptoms suggesting metastasis. Bone scan was performed if the patient is complaining of localized bony tenderness. All the patients who received Tamoxifene performed gynecological examination and pelvic U/S annually to assess the endometrial thickness. Patient who received Aromatase inhibitors were monitored for bone health by annual osteo-densitometry (DEXA scan).

RESULTS:

This analysis was based on the data of 60 female patients with newly diagnosed early breast cancer patients according to TNM staging system. The age among the patients of this study ranged from 39-60 years, with 51.7% negative hormonal status and 48.3% positive, as shown in table (1).

cases ranged between 28%-83% and during follow up after receiving neoadjuvant therapy we noticed significant reduction among the studied cases as shown in table (2).

Table (2) shows that: **Ki-67** significantly decreased at follow up among the studied cases.

The initial tumor size among the cases ranged between 0.8-4.8 cm and showed

significant decrease at follow up after receiving first cycle of chemotherapy or 2 months hormonal therapy among the studied cases.

Table (3): Tumor size (cm) among the studied cases.

Time	Mean ± SD	Range	^p-value
Baseline	2.4±1.2	0.8–4.8	<0.001*
Follow up	1.4±1.3	0.0–5.2	
Change percent	-49.3±41.7	-100.0–48.6	

Total=60. Change = After – before, negative values indicate reduction. ^Paired t-test. *Significant

Table (3) shows that: **Tumor size** significantly decreased at follow up among the studied cases.

patients) developed partial response, 10 patients had stable disease while the remaining 6 cases showed progressive response after receiving neoadjuvant therapy.

Seven of our patients achieved PCR while the majority of our studied cases (37

Table (4): Clinical response among the studied cases

Response	N	%
Complete response	7	11.7
Partial response	37	61.7
Stable disease	10	16.7
Progressive response	6	10.0

Total=60

Table (4) show that: **Partial response** was the most frequent among the studied cases.

regarding age, hormonal status and baseline tumour size, there were no statistical significant differences

During comparing the clinical response

Table (5): Comparison according to clinical response regarding age, hormone status and baseline tumor size

Variables		Complete response (N=7)	Partial response (N=37)	Stable disease (N=10)	Progressive response (N=6)	p-value
Age (years)		46.3±3.1	48.8±5.9	48.0±6.3	48.7±4.6	^0.750
Hormone status	Positive	4 (57.1%)	18 (48.6%)	5 (50.0%)	2 (33.3%)	#0.903
	Negative	3 (42.9%)	19 (51.4%)	5 (50.0%)	4 (66.7%)	
Baseline tumor size (cm)		1.9±0.8	2.3±1.2	3.3±1.0	2.3±1.1	^0.077

^ANOVA test. #Fisher's Exact test

Table (5) shows that: No statistical significant differences according to clinical

response regarding **age, hormone status and baseline tumor size.**

Table (6): Comparison according to clinical response regarding Ki-67 (%)

Time	Complete response (N=7)	Partial response (N=37)	Stable disease (N=10)	Progressive response (N=6)	^p-value (responses)
Baseline	44.0±8.4	52.5±11.7	64.3±12.4	74.8±7.0	<0.001*
Follow up	22.3±9.2	34.5±16.1	53.9±23.1	74.6±15.0	<0.001*
Change percent	-51.2±11.5	-37.9±17.2	-19.0±17.1	-1.2±12.0	<0.001*
#p-value (times)	<0.001*	<0.001*	0.015*	0.958	

Change = After – before, negative values indicate reduction. ^ANOVA test. #Paired t-test. *Significant

Table (6) shows that: **Baseline and follow up Ki-67** was lowest in complete response, followed by partial response, then stable disease and highest in progressive response, the differences statistically were significant. **Change percent of Ki-67** was highest in complete response, followed by

partial response, then stable disease and lowest in progressive response, the differences statistically were significant. **Ki-67** significantly decreased in complete response, partial response and stable disease and non-significantly changed in progressive response.

Table (7): Diagnostic performance of Ki-67 in predicting clinical responses

Item	Complete from worser	Partial from worser	Progressive from better
AUC	0.803	0.831	0.935
p-value	0.010*	<0.001*	<0.001*
Cut point	≤51.0%	≤57.5%	≥72.0%
Sensitivity	85.7%	75.7%	83.3%
Specificity	75.5%	81.3%	92.6%
Diagnostic accuracy	76.7%	77.4%	91.7%
Positive predictive value	31.6%	90.3%	55.6%
Negative predictive value	97.6%	59.1%	98.0%

AUC: Area under curve. *significant

Table (7): **Ki-67** statistically had significant moderate diagnostic performance in predicting **clinical responses**, was highest in predicting **progressive response**.

Another tru-cut biopsy was taken on the 15th to 20th day after the 1st cycle of chemotherapy and after 2 months (the 60th day) after starting the hormonal treatment to re-measure the Ki 67 index.

DISCUSSION:

In this study, we aimed to evaluate the response rate to neoadjuvant chemotherapy or hormonal therapy in cases of early breast cancer (T1, T2-N0, N1-M0) according to the TNM staging and to find the predictive value of the reduction of the prognostic value Ki-67 for the response to the neo-adjuvant treatment.

During the follow-up of the patients, the current study results revealed that Ki-67 was significantly decreased with significantly decreased tumor size at follow up among the studied cases (*p*<0.001).

This prospective study was conducted at tertiary care hospital at the breast surgery unit and clinical oncology departments, Ain Shams University Hospitals from 2015 till 2017 and performed on a total of 60 female patients with newly diagnosed early breast cancer patients according to TNM staging system.

As regards the clinical response after neoadjuvant chemotherapy, the current study results revealed that Partial response was the most frequent among the studied cases with no statistically significant differences according to clinical response regarding age, hormone status and baseline tumor size.

The female patients involved in the study received neo-adjuvant chemotherapy or hormonal therapy if required in treating operable and early detected breast cancer patients.

Baseline and follow up Ki-67 were lowest in complete response, followed by partial response, then stable disease and highest in progressive response, the differences statistically were significant.

Consequently, change percent of Ki-67 were highest in complete response, followed by partial response, then stable disease and lowest in progressive response, the differences statistically were significant. Ki-67 significantly decreased in complete

response, partial response and stable disease and non-significantly changed in progressive response ($p < 0.001$).

As a result, Ki-67 statistically had significant moderate diagnostic performance in predicting clinical responses, was highest in predicting progressive response.

Ki-67 has been assayed in many studies as a prognostic and/or predictive marker in early BC. As a predictive marker, very few trials of primary systemic therapy, mostly retrospective and with conflicting results have been published⁽²⁰⁾, and therefore we felt that the assessment of the predictive role of Ki-67 was out of scope for this study.

Maranta et al.,⁽²¹⁾ conducted a retrospective study to evaluate the robustness of Ki-67 values within one center over 5 years and to compare its distribution with a published dataset of breast cancer and reported that Ki-67 values correlated with tumor grade, with higher grades having higher Ki-67 values. The standard deviation of Ki-67 increases with higher grading. (G1: 6.9; G2: 9.2; G3: 18.2). The differences in distributions were highly significant ($p < 0.001$).

De Azambuja et al.⁽²²⁾ conducted a systematic review that enrolled Sixty-eight studies including 12155 patients to better define the prognostic value of Ki-67/MIB-1 on disease-free survival (DFS) and/or on overall survival (OS) in early BC and revealed that Ki-67 positivity is associated with higher probability of relapse and worse survival in all patients with early BC.

Inwald et al.,⁽²³⁾ conducted a retrospective study that enrolled a total of 3,658 patients with invasive breast cancer and reported that Ki-67 expression was associated with the common histopathological parameters. The strongest correlation was found between grading and Ki-67 ($P < 0.001$).

On the contrary, *Ragab et al.*,⁽²⁴⁾ conducted a retrospective study that included

92 patients with developed non metastatic breast cancer and 10 women had benign breast tumor served as controls to evaluate the value of Ki-67 as a prognostic marker in breast cancer patients and to analyze the associations between Ki-67 and their clinicopathological parameters and revealed that there were no statistically significant differences in serum Ki-67 levels between the two studied groups.

While for Ki-67 expression in breast cancer cells, the score increases with increase of tumor size, grade, premenopausal, Ki-67 expression in estrogen and progesterone receptor positive tumors showed lower values than estrogen and progesterone negative tumors⁽²⁴⁾.

These results were in agreement our results and with *Fausto et al.*,⁽²⁵⁾ who stated that high immunohistochemical expression Ki-67 level is associated with greater risk of recurrence (64 % increased risk) and that the proliferative marker Ki-67 has an independent prognostic value in terms of survival and relapse in patients with early-stage breast cancer (BC), and should be routinely assessed by pathologists.

Nishimura et al.,⁽²⁶⁾ demonstrated that high Ki-67 in primary tumors, irrespective of high or low Ki-67 in recurrent tumors, was significantly correlated with a lower survival rate, although, *Ibrahim et al.*⁽²⁷⁾ reported that patients with high Ki-67 in recurrent tumors showed significantly lower survival rates, irrespective of high or low Ki-67 in primary tumors. Another study investigated the relationship between proliferation markers and patient survival confirmed that high Ki-67 is associated with worse survival rate⁽²⁸⁾.

The strength points of this study are that it is prospective study design, its setting at a single tertiary care center and having no patients lost to follow-up in three months. It is the first study in Ain Shams University Hospitals to evaluate the proliferation marker Ki-67 which is one of the most

controversially discussed parameters for treatment decisions in breast cancer patient⁽²¹⁾.

Conclusion:

As evident from the current study, Ki-67 is a valuable marker, as it has prognostic and predictive abilities after neoadjuvant chemotherapy. Ki-67 expression may be considered a valuable potential biomarker and add a prognostic information to that obtained from classical prognostic factors such as tumor size.

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تقييم العلاج ما قبل الجراحي في حالات سرطان الثدي المتقدمة محلياً وارتباطه بالمؤشر التنبؤي Ki67

منار شعبان صالح* - رضا عبد التواب خليل** - اشرف عبد المغني مصطفى* - هاني عبد العزيز*** -
لبنى شاش**** - ياسر محمد عبد السميع**

* قسم الجراحة العامة - الإسماعيلية

** قسم الجراحة العامة - كلية الطب - جامعة عين شمس

*** قسم العلاج الكيميائي والاشعاعي - كلية الطب - جامعة عين شمس

**** قسم الباثولوجي - كلية الطب - جامعة عين شمس

مقدمة: كان سرطان الثدي أكثر أنواع السرطانات التي يتم تشخيصها والسبب الرئيسي للوفيات بسبب السرطان لدى الإناث، حيث يمثل 23% (1.38 مليون) من إجمالي حالات السرطان الجديدة و 14% (458,400) من إجمالي وفيات السرطان في عام 2010. حوالي نصف الثدي تشير التقديرات إلى حدوث حالات السرطان و 60% من الوفيات في البلدان النامية اقتصادياً.

الهدف من العمل: تقييم معدل الاستجابة للعلاج الكيميائي المساعد الجديد أو العلاج الهرموني في حالات سرطان الثدي المبكر (T1 ، T2-N0 ، N1-M0) وفقاً لتصنيف TNM وإيجاد القيمة التنبؤية لتقليل قيمة النذير Ki-67 للاستجابة للعلاج المساعد الجديد.

المرضى وطرق البحث: أجريت هذه الدراسة المستقبلية في مستشفى الرعاية الثالثة في أقسام الجراحة العامة والأورام السريرية بمستشفيات جامعة عين شمس من عام 2015 حتى عام 2017 وأجريت على إجمالي 60 مريضة مصابات بسرطان الثدي تم تشخيصهن حديثاً وفقاً لنظام TNM.

النتائج: فيما يتعلق بالاستجابة السريرية بعد العلاج الكيميائي المساعد الجديد ، أظهرت نتائج الدراسة الحالية أن الاستجابة الجزئية كانت الأكثر تكراراً بين الحالات المدروسة مع عدم وجود فروق ذات دلالة إحصائية وفقاً للاستجابة السريرية فيما يتعلق بالعمر والحالة الهرمونية وحجم الورم الأساسي. نتيجة لذلك ، كان Ki-67 إحصائياً أداء تشخيصي معتدل معتدل في توقع الاستجابات السريرية، وكان الأعلى في توقع الاستجابة التقدمية.

الخلاصة: خلصنا إلى أن Ki-67 هو علامة قيمة ، لأنه يتمتع بقدرات تنبؤية وتنبؤية بعد العلاج الكيميائي المساعد الجديد. يمكن اعتبار تعبير Ki-67 علامة حيوية محتملة ذات قيمة وإضافة معلومات تنبؤية لتلك التي تم الحصول عليها من عوامل الإنذار الكلاسيكية مثل حجم الورم.