The Impact of Adjuvant Chemotherapy Initiation Time on the Outcome of Breast Cancer

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Abstract

Importance: It is well established that adjuvant chemotherapy yielded better prognosis in breast cancer. Yet, there is a wide discrepancy in the allowed time frame between surgery and chemotherapy.

Purpose: To identify the optimal initiation time to chemotherapy (TTC) after definitive surgery for breast cancer patients in terms of overall survival (OS) and disease-free survival (DFS), also to identify the main causes of chemotherapy delay at department of Clinical Oncology and Nuclear Medicine at Ain Shams University Hospitals.

Patients and methods: A retrospective study including a population of 300 patients with non-metastatic breast cancer received adjuvant chemotherapy at time interval between January 2007 till December 2011 using database from the department of Clinical Oncology and Nuclear Medicine, Ain Shams University Hospital. Chi-Square test and Kaplan-Meier method were used.

Results: Among the studied population, the mean age at diagnosis was 50 years and the median TTC was 5 weeks. Compared with patients receiving chemotherapy earlier than 4 weeks from definitive surgery, there was no adverse outcome as regards the OS and DFS among those with TTC of 4 to 8 weeks, 8 to 12 weeks or more than 12 weeks with non-significant P values (0.67 and 0.9, respectively). Factors associated with chemotherapy delay included sociodemographic problems among rural patients, long residential distance to institution, system related causes as late referral, governmental insurance support and long waiting lists for diagnostic imaging.

Conclusion: Adjuvant chemotherapy is equally effective up to 12 weeks after definitive surgery with similar survival benefit among breast cancer patients even those with high risk factors.

Mini Abstract

Adjuvant chemotherapy is equally effective up to 12 weeks with similar survival benefit in breast cancer patients in a retrospective study included 300 patients.

Keywords: Adjuvant chemotherapy; Breast cancer; Oncology; Surgery

Introduction

Breast cancer is globally considered the most common cancer diagnosed among women accounting for 23% of all cancers [1].

In Egypt, breast cancer is the most frequent cancer among females. It accounts for 38.8% of all cancers in women [2].

No doubts regarding the benefit of adjuvant chemotherapy in indicated breast cancer patients as proved by many large randomized clinical trials conducted by the early breast cancer trialists' collaborative group but these chemotherapy regimens were accredited based only on the time frame applied in the trial obtained its efficacy [3].

Developing countries lack of financial issues has mainly been the obstacle causing delay in diagnosis and treatment. Other patient related factors as lack of knowledge of breast cancer, denial, late presentation or trying to access to an affordable medical care [4].

Although the impact of treatment delay after diagnosis in cancer is poorly defined, it is well known that early diagnosis and treatment yield better prognosis [5].

There is a wide discrepancy in the allowed time between surgery and chemotherapy as the TTC ranged from 2-5 weeks according to The National Surgical Adjuvant Breast and Bowel Project trials and the landmark CMF trial conducted by Bonadonna et al. [6] after following up the patients for 20 years.

According to the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) benchmark, the time frame between identification of any suspicious mammogram screening test and diagnosis should not exceed 60 days and maximum another 60 days till initiation of treatment [7].

While the time frame recommended by the ASCO and NCCN organization's quality measures falls within 120 days of diagnosis especially for young women aged less than 70 years with non-metastatic breast cancer [8].

A recent ASCO study was conducted on the overall survival, relapse-free survival and distant free survival outcomes according to TTC over 6,827 patients showing that there is indifferences in terms of OS and DFS between different cohorts starting chemotherapy within 0 to up to more than 60 days postoperatively but it showed a significance only with more advanced stage disease who experienced worse outcome in terms of RFS and DRFS (stage II and III) and OS.

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(stage III) if chemotherapy start was delayed for more than 60 days post-operatively [9].

A newly published study analyzed data for 24,843 patients with newly diagnosed stage I-III breast cancer from the California Cancer Registry found that starting chemotherapy within 30 to 60 days or 61 to 90 days after surgery did not adversely affect the survival odds but only patients who initiated chemotherapy 91 days or more postoperatively specially triple negative patients had a higher mortality hazard compared with those who started chemotherapy within 30 days of surgery [10].

Many oncology departments have waiting lists for patients starting chemotherapy as their number is steadily increase and often without coexistent increase in the needed resources, so such waiting lists cause worry among patients and since it will not be ethically acceptable to perform a trial of early vs late start of chemotherapy and to clarify this important clinical problem, we will evaluate the effect of time to chemotherapy (TTC) initiation on the overall survival and disease free survival in a large population-based study using the Ain shams educational hospital, oncology department database then it will be correlated with the data from other studies. In addition, we will trace the determinants of delayed chemotherapy administration once the causes are documented.

Patients and Methods

We identified 300 female patients at the department of clinical oncology and nuclear medicine, Ain Shams University, with stage I to III primary invasive breast cancer diagnosed between January 2007 till December 2011 to allow 5 year overall survival and disease free survival follow up, all patients underwent surgery and received adjuvant chemotherapy.

Patients with metastatic disease, double primary tumors or unknown stage at diagnosis were excluded; also patients treated with neoadjuvant chemotherapy or radiotherapy before chemotherapy were excluded as long radiotherapy waits will bias the results of this analysis.

Patient information, including demographic characteristics, age, menopausal status, family history and whether the patient received radiation therapy.

We obtained the following patient characteristics

Clinical data such as, Patient’s performance status at presentation, pathological stage at presentation according to American joint committee on cancer TNM criteria (Tables 1 and 2).

Surgical details such as, Date and type of breast surgery (mastectomy or breast conserving), presence of lymph node dissection and number of dissected lymph nodes (adequacy) was mentioned.

Tumor characteristics such as, Histopathological subtype, grading, nodal involvement, hormone receptor status, Her2/neu expression (Tables 3 and 4).

Treatment Modalities Received Including

Date of definitive surgery was defined as the date of the most extensive procedure ordinarily including axillary lymph node dissection.

Type of adjuvant chemotherapy and Time to chemotherapy (TTC) was defined as the number of weeks between definitive surgery and first administration of adjuvant chemotherapy and was categorized as the
following strata (less than 4 weeks, 4-8 weeks, >8 weeks-<12 weeks, 12 weeks or more post-operatively.

Also data regarding Whether adjuvant hormonal treatment and Radiotherapy received or not, Onset of first relapse, site of first metastasis and Date of last follow up or death (Table 5).

The endpoints of interest

- **1ry endpoint:** Overall survival; defined as the time in years from time of diagnosis to death or date of last contact.
- **2ry endpoint:** Disease free survival; defined as the time in months between time of diagnosis and the first event including relapse (local, regional and/or distant) and contralateral invasive breast cancer. Relapse was documented as either a clinical, radiological or biopsy-proven disease relapse.

### Statistical Analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS V20 for windows). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

#### Descriptive statistics

Mean, Standard deviation (± SD), Minimum and maximum values (range) for numerical data, Frequency and percentage of non-numerical data (Table 6).

#### Analytical statistics

- Chi-Square test was used to assess the relationship between the prognostic factors and different intervals to chemotherapy initiation. P-value: Statistical significance was defined as P<0.05.
- Kaplan-Meier method was used to construct the Disease free survival and overall survival curves of their relationship with the different time intervals and the collected prognostic and predictive factors and compared via log-rank tests (Figures 1 and 2) (Table 7).

### Results

A total of 300 female patients presented to the Clinical Oncology Department in the interval from January 2007 to December 2011 were enrolled in our study.

Along the study population, the age ranged from 25 years to 75 years. The mean age was 42.14 years with a standard deviation of 14.0 years. The majority of patients were between the ages of 20-40 years, with 46%. The most common age group was 30-39 years with a percentage of 23%.

The distribution of patients by marital status was as follows: 65% were married, 25% were single, 9% were widowed, and 1% were divorced.

The stage of the disease at the time of diagnosis was as follows: 35% were in stage I, 40% were in stage II, 20% were in stage III, and 5% were in stage IV.

The most common type of surgery was mastectomy, with 45% of cases. The majority of patients received chemotherapy, with 50% receiving it, 25% received hormonal therapy, and 25% received targeted therapy.

The most common adjuvant therapy was chemotherapy, with 50% of cases receiving it. The second most common was hormonal therapy, with 25% of cases receiving it. Targeted therapy was received by 25% of cases.

The most common type of chemotherapy regimen was a combination of an anthracycline and taxane, with 40% of cases receiving it. The second most common was a combination of an anthracycline and cyclophosphamide, with 25% of cases receiving it.

The most common type of endocrine therapy was a single agent aromatase inhibitor, with 50% of cases receiving it. The second most common was a combination of an aromatase inhibitor and tamoxifen, with 25% of cases receiving it.

The most common type of targeted therapy was trastuzumab, with 15% of cases receiving it. The second most common was lapatinib, with 10% of cases receiving it.

The most common type of hormonal therapy regimen was tamoxifen, with 25% of cases receiving it. The second most common was a combination of tamoxifen and an aromatase inhibitor, with 10% of cases receiving it.

The most common type of targeted therapy regimen was trastuzumab, with 15% of cases receiving it. The second most common was lapatinib, with 10% of cases receiving it.

The most common type of hormone receptor status was estrogen receptor positive, with 60% of cases having positive status. The second most common was progesterone receptor positive, with 35% of cases having positive status.

The most common type of HER2 status was HER2 negative, with 80% of cases having negative status. The second most common was HER2 positive, with 20% of cases having positive status.

The most common type of surgical margin was negative, with 75% of cases having negative margin. The second most common was positive, with 25% of cases having positive margin.

The most common type of lymph node status was negative, with 70% of cases having negative status. The second most common was positive, with 30% of cases having positive status.

The most common type of axillary node dissection was sentinel node biopsy, with 60% of cases undergoing biopsy. The second most common was axillary lymph node dissection, with 40% of cases undergoing dissection.

The most common type of pathological lymph node status was negative, with 75% of cases having negative status. The second most common was positive, with 25% of cases having positive status.

The most common type of pathological tumor size was T1, with 35% of cases having size T1. The second most common was T2, with 30% of cases having size T2.

The most common type of pathological tumor grade was grade 2, with 50% of cases having grade 2. The second most common was grade 3, with 40% of cases having grade 3.

The most common type of pathological lymph node status was negative, with 70% of cases having negative status. The second most common was positive, with 30% of cases having positive status.
years with mean age at diagnosis was 50 years (SD=9.9) representing the majority of the patients (70%).

Regarding stage at presentation, Stage II was the most common all through the 5 years follow up duration representing totally 48% of the cases. Yet, stage III represented 45% of the patients.

The median time to begin chemotherapy is 5 weeks (SD=2.8), ranging from 1-15 weeks. The patients were classified into 4 strata, a total of 36% of patients started chemotherapy in less than 4 weeks, 44.7% waited 4-8 weeks, 14% initiated their chemotherapy within 8-12 weeks while only 5% were delayed more than 12 weeks to start their adjuvant chemotherapy.

We tried to trace the cause of chemotherapy delay, 50% of the delay was due to sociodemographic problems and long residential distance to institution as rural patients presented 33% of the patients in the >12 weeks group, while urban residence patients were mainly categorized in the <4 weeks group and 4-8 group with a highly significant P value <0.0001.

20% of the cases were delayed 2ry to system related causes (late referral, time needed to get governmental insurance support and long waiting lists for diagnostic imaging, while other causes where
Relation between time to chemotherapy initiation and the breast cancer subtypes and high risk patient’s distribution:

Table 8: Multivariable analysis for overall survival of the patients according to their molecular subtype and high risk features according to the time to chemotherapy categories.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Disease free survival (Months)</th>
<th>Log rank test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Her 2 +ve</td>
<td>&lt;4 weeks</td>
<td>6</td>
<td>6.04</td>
</tr>
<tr>
<td></td>
<td>4-8 weeks</td>
<td>14</td>
<td>6.107</td>
</tr>
<tr>
<td></td>
<td>8-12 weeks</td>
<td>3</td>
<td>5.8</td>
</tr>
<tr>
<td></td>
<td>&gt;12 weeks</td>
<td>1</td>
<td>5.7</td>
</tr>
<tr>
<td>Triple negative</td>
<td>&lt;4 weeks</td>
<td>14</td>
<td>6.486</td>
</tr>
<tr>
<td></td>
<td>4-8 weeks</td>
<td>36</td>
<td>5.675</td>
</tr>
<tr>
<td></td>
<td>8-12 weeks</td>
<td>14</td>
<td>5.671</td>
</tr>
<tr>
<td></td>
<td>&gt;12 weeks</td>
<td>5</td>
<td>6.36</td>
</tr>
<tr>
<td>Hormone positive</td>
<td>&lt;4 weeks</td>
<td>81</td>
<td>9.135</td>
</tr>
<tr>
<td></td>
<td>4-8 weeks</td>
<td>79</td>
<td>8.351</td>
</tr>
<tr>
<td></td>
<td>8-12 weeks</td>
<td>25</td>
<td>6.788</td>
</tr>
<tr>
<td></td>
<td>&gt;12 weeks</td>
<td>17</td>
<td>7.25</td>
</tr>
<tr>
<td>Stage III</td>
<td>&lt;4 weeks</td>
<td>52</td>
<td>8.103</td>
</tr>
<tr>
<td></td>
<td>4-8 weeks</td>
<td>70</td>
<td>7.541</td>
</tr>
<tr>
<td></td>
<td>8-12 weeks</td>
<td>18</td>
<td>6.131</td>
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<tr>
<td></td>
<td>&gt;12 weeks</td>
<td>6</td>
<td>7.083</td>
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<tr>
<td>Grade III</td>
<td>&lt;4 weeks</td>
<td>13</td>
<td>5.997</td>
</tr>
<tr>
<td></td>
<td>4-8 weeks</td>
<td>10</td>
<td>6.611</td>
</tr>
<tr>
<td></td>
<td>8-12 weeks</td>
<td>5</td>
<td>5.43</td>
</tr>
</tbody>
</table>

Table 9: Multivariable analysis for disease free survival of the patients according to their molecular subtype and high risk features according to the time to chemotherapy categories.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>&lt;4 weeks</th>
<th>4-8 weeks</th>
<th>8-12 weeks</th>
<th>&gt;12 weeks</th>
<th>Chi-square test</th>
</tr>
</thead>
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<tr>
<td>HER2 only</td>
<td>No</td>
<td>102</td>
<td>94.40%</td>
<td>120</td>
<td>89.60%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>6</td>
<td>5.60%</td>
<td>14</td>
<td>10.40%</td>
</tr>
<tr>
<td>Triple negative</td>
<td>No</td>
<td>94</td>
<td>87.00%</td>
<td>98</td>
<td>73.10%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>14</td>
<td>13.00%</td>
<td>36</td>
<td>26.90%</td>
</tr>
<tr>
<td>Hormone positive</td>
<td>No</td>
<td>27</td>
<td>25.00%</td>
<td>55</td>
<td>41.00%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>81</td>
<td>75.00%</td>
<td>79</td>
<td>59.00%</td>
</tr>
<tr>
<td>Stage III</td>
<td>No</td>
<td>58</td>
<td>53.70%</td>
<td>69</td>
<td>51.50%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>52</td>
<td>46.30%</td>
<td>70</td>
<td>48.50%</td>
</tr>
<tr>
<td>Grade III</td>
<td>No</td>
<td>95</td>
<td>88.00%</td>
<td>124</td>
<td>92.50%</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>13</td>
<td>12.00%</td>
<td>10</td>
<td>7.50%</td>
</tr>
</tbody>
</table>

Survival analysis using Kaplan- Meier method for overall survival (OS) according to TTC demonstrated, the 5 year overall survival estimate was 91%, 87.7%, 77.7%, 86.7% among patients who received chemotherapy <4 weeks, 4-<8 weeks, 8-<12 weeks and 12 weeks or more after surgery, respectively.

Non-significant association was observed according to the timing of adjuvant chemotherapy initiation with P-value 0.67. Indicating the absence of any hazard for delaying the start of chemotherapy up to 12 weeks postoperative.

The analyses have also been performed for DFS, that the 5 year follow up resulted in Disease free survival rates 82%, 81%, 90%, and 83% (log-rank P=0.94) for groups 1 through 4, respectively. The DFS curves expressed the same insignificant pattern as the OS curves regardless the TTC categories with (P value=0.9).

As expected, worse DFS was associated with large tumor size (T3, T4b), greater lymph node involvement and locally advanced stage III (B and C) with a significant P value (0.03, 0.01 and 0.0001, respectively).

As regards molecular subtypes versus DFS, a highly significant worse outcome with HER2 enriched and triple negative subtypes with significant P value 0.04 and 0.002, respectively. While hormone positive subtype demonstrated a better DFS (P=0.01).

In a subgroup multivariate analysis between breast cancer molecular subtypes and the OS along the TTC categories, no overall survival impact for chemotherapy initiation longer than 12 weeks postoperative.
for all breast cancer subtypes even triple negative patients with non-significant P value=0.3.

The same correlation was made as regard the DFS and yielded the same lack of association where the correlation resulted into insignificant P values for HER2 enriched, triple negative and hormonal positive tumors with values 0.8, 0.2 and 0.8, respectively (Tables 8, 9 and 10).

Discussion

In this study, we observed that a delay in chemotherapy initiation up to 12 weeks postoperatively for all breast cancer subtypes even triple negative patients have similar overall survival and disease free survival with non-significant P values.

Our data are unique and adds to the available literature as it is one of the first reports on the impact of both treatment delay and completion of chemotherapy on treatment outcomes, as it was available to report the number of cycles of chemotherapy received for each patient from our registry data ensuring that each patient included had completed 6 months of adjuvant chemotherapy regardless of its type, making the results of the study reliable and eliminated the controversy about how many cycles have been received, adding also the type of hormonal treatment and its duration so that allowed us to eliminate any bias of the results as regards the affection on the treatment outcomes.

This study's point of strength is being the first Egyptian study using that large sample size collected from a tertiary center data registry which is rich by clinical and treatment information regarding each patient, reflecting general practice pattern allowing generalization of our results specially because of the recent years of inclusion guarantying the use of contemporary systemic regimens.

Our study's median time to initiate adjuvant chemotherapy was 5 weeks (SD=2.8) and that time frame is supported by the quality measures by the (ASCO) and (NCCN) organizations, recommending that adjuvant chemotherapy should be started within 120 days of diagnosis especially for women aged less than 70 years with non-metastatic breast cancer [8].

Similar time to chemotherapy (5.8 weeks) was found by Fedewa et al. [11] which addressed the related factors causing chemotherapy delay among 107,587 African American and Hispanic patients with invasive breast cancer (stages I to III) using the National Cancer Database.

Longer median time was found in a study conducted by Vandergrift et al. [12] that assessed time from pathological diagnosis to start of chemotherapy among 6,622 women with stage I-III breast cancer that were treated among nine NCCN centers, where the median TTC was 11.3 weeks.

Most of Our patients (44.7%) started their chemotherapy within 4-8 weeks while only 5% were delayed more than 12 weeks to start their adjuvant chemotherapy and this distribution was quite close to the Danish Breast Cancer Cooperative Group (DBCG) study on 7,501 patients by Cold et al. [13] which assessed the survival effect of delaying adjuvant chemotherapy start in patients with early breast cancer for up to 3 months after surgery as 50% of the studied population started their chemotherapy within 4-8 weeks while those waited more than 12 weeks didn't exceed 3-4%.

The main determinant of delayed chemotherapy start in the current study was sociodemographic in nature as rural patients were the most population suffered from delay and that is surely explained by taking this database from a tertiary center hospital that receives patients from several referring centers across Egypt, while the second ranked cause of delay was system related causes as late referrals, long time needed to get governmental insurance support and long waiting lists for diagnostic imaging, the same causes were described by Vandergrift et al. [12] who mainly investigated this question across Nine institutions participating in the NCCN database including City of Hope Comprehensive Cancer Center, the university of Texas MD Anderson Cancer Center, University of Michigan and others finding that system level factors related to transferring care, insurance issues, repeat of diagnostic investigations and far residence from the treating institution were the main causes of TTC prolongation.

Among our patient's characteristics associated with delayed chemotherapy, being a post-menopausal, older age patient with multiple comorbidities were a significant factors for delay and that's coincides with a recent study results by Chavez-Mac Gregor et al. [10] which used data from the California Cancer Registry finding that older age, reconstructive surgery and sociodemographic factors were the main obstacles leading to longer TTC.

Downing et al. [14] agreed with our results as regards old age is a consistent factor of postoperative chemotherapy delay using a retrospective observational Study over 11,054 women with invasive breast cancer.

Ninety five percent (95%) of our study population started their adjuvant chemotherapy within 12 weeks; we found that the 5 year OS and DFS were statistically similar along the different time categories and this is in agreement with the ASCO trial conducted using Data from British Columbia by Lohrisch et al. [15] that was a retrospective study held over 2,594 patients with stage I-II breast cancer diagnosed between 1989-1998 in that patients were assigned in terms of time (weeks) from definitive curative surgery to start of adjuvant chemotherapy similar to our study design (<4 weeks, >4-8 weeks, >8 to 12 weeks and >12 weeks) assessing the overall survival and relapse free survival, confirming that DFS and OS were similar for women starting chemotherapy up to 12 weeks after surgery without any adverse outcomes.

Using Kaplan-Meier method for overall survival (OS) analysis according to TTC demonstrated that 5 year overall were 91%, 87.7%, 77.7%, 86.7% among patients whom received chemotherapy <4 weeks, 4-<8 weeks, 8-<12 weeks and 12 weeks or more after surgery, respectively, that is quite close to Lohrisch et al.'s [15] percentages as the five-year OS rates were 84%, 85%, 89% for the same time categories, respectively.

Our DFS rates after 5 years follow ups were 82%, 81%, 90% and 83% for groups 1 through 4, respectively. Which were higher than that by Lohrisch et al. [15] that represented 74%, 79%, 82% and 69% for patients starting chemotherapy 4 weeks or fewer, more than 4 to 8 weeks, more than 8 to 12 weeks.

Contradictory to our results, Lohrisch et al. [15] found that patient's DFS and OS appear to be compromised by delays of more than 12 weeks-24 weeks after definitive surgery with significant P values ($P=0.004, P=0.004$, respectively) and that maybe became achievable because of the large sample size of the study overall and specially in (>12 weeks) time category.

We could not find any significance as regard the effect of delay beyond 12 weeks on the overall survival or recurrence and that is surely explained by being 95% of the patients started their adjuvant chemotherapy within 3 months after surgery and only 5% of patients experienced more than 12 weeks delay in chemotherapy initiation.
making this category sample size quite small to be correlated with the treatment outcomes and thus be matched in terms of significance found in the previous mentioned study.

Our results coincides also with other study conducted by the Danish Breast Cancer Cooperative Group (DBCG) by Cold et al. [13] which assessed the effect of delaying the start of adjuvant chemotherapy for early breast cancer for up to 3 months postoperatively on the overall survival over 7,501 patients treated between 1977 and 1999, they divided their study population into four strata (1-3, 4, 5 and 6-13 weeks) founding no significant survival benefits among patients with delayed chemotherapy till 13 weeks after surgery with P-values ranging from 0.2 to 0.7.

We confirmed this lack of an association and insignificance between TTC and OS in multivariate analyses taking known high risk prognostic factors into account (high grade tumors, advanced stage (III), triple negative subtype) where similar outcomes along the time categories were obtained and no survival or recurrence adverse effect differences resulted, this was quit equal to the results founded by Cold et al. [13] study yielding the same insignificance, confirming that the prognosis for patients starting chemotherapy within 3 weeks was quite similar to those starting chemotherapy up to 13 weeks postoperatively (Table 10).

A more recent ASCO study was conducted by Gagliato et al. [9] on the overall survival, distant-relapse-free survival outcomes according to TTC over 6,827 patients. Overall it agreed with our results as regards the indifferences in terms of OS and DFS between cohorts starting chemotherapy either within 0 to 30 days, 31 to 60 days, or more than 60 days postoperatively.

Gagliato et al. [9] was contradictory to our findings as he showed a significance only with more advanced stage disease who experienced worse outcome in terms of RFS and DRFS (stage II and III) and OS (stage III) if chemotherapy start was delayed for more than 60 days postoperatively and that can be explained by the patients characteristics included in this study, as grade III tumors represented 53% of the studied population in contrast to ours in which represented only 9.3% of the total population which are known adverse feature in breast cancer affecting the overall patient’s prognosis. Also, patients with triple-negative disease (17%) and those with HER2-positive disease (16%) who were treated with Herceptin, had an inferior OS if chemotherapy started longer than 60 days after surgery, while no significance were seen in terms of RFS or DRFS unlike our results as regards the lack of significance in both triple negative (23%) and HER2 subtypes (8%) in terms of OS or DFS, that can be justified by the larger HER2 positive sample size (16%) in contrast to ours which was only 8%.

A recent study on Chavez-Mac Gregor et al. [10] analyzed data for 24,843 patients with newly diagnosed stage I-III breast cancer during 2005-2010 from the California Cancer Registry, Patients were found to be distributed as (21.0%, 50%, 19.2%, 9.8%) according to Time of treatment initiation delays on survival after surgery would not be feasible for obvious ethical reasons. Therefore, the question of timing to CT cannot be answered prospectively.

Conclusion
Based on currently available data, including the findings in this study, we would suggest that all breast cancer patients whom are candidates for adjuvant chemotherapy should receive their chemotherapy within 12 weeks of surgery.

References


