

A Retrospective Study on Previously Untreated Non-metastatic Breast Cancer Patients at a Tertiary Care Hospital

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Abstract

Introduction: The combination of adoxorubicin and cyclophosphamide (AC) followed by a taxane (Docetaxel or Paclitaxel) and epirubicin and cyclophosphamide (EC) followed by a taxane (Docetaxel or Paclitaxel) is a standard regimen for breast cancer patients. In this study, we compared the three-year overall survival (OS) and progression free survival (PFS) of a patient with previously untreated non-metastatic breast cancer patients.

Objectives: To find out the overall survival and progression free survival among previously untreated non-metastatic breast cancer patients after standard chemotherapy.

Methods: Fifty-six patients received four cycles of doxorubicin at a dose of 60mg/m² and cyclophosphamide at a dose of 600 mg/m² followed by four cycles of paclitaxel at a dose of 175mg/m². Thirteen patients received AC followed by four cycles of docetaxel at a dose of 75mg/m². Twenty-one patients received four cycles of epirubicin (75mg/m²) and cyclophosphamide (600mg/m²), followed by four cycles of paclitaxel (175mg/m²). Twelve patients were given EC followed by four cycles of docetaxel (75mg/m²).

Results: The four groups of patients had similar characteristics. Overall survival after three years was 92% in AC followed by paclitaxel, 98% in AC followed by docetaxel, 95% and 97% in EC followed by paclitaxel and docetaxel respectively. One year of PFS in AC followed by paclitaxel and docetaxel was 98% and 100% respectively whereas in EC followed by paclitaxel and docetaxel were 98% and 98% respectively. The four arms had 96%, 98%, 97% and 96% PFS after two years respectively. This research also revealed that four chemotherapy regimens had three-year survival rates of 93%, 98%, 93% and 96% respectively.

Conclusion: AC or EC followed by taxane regimens well suitable regimens for the population of patients with

previously untreated non-metastatic breast cancer patients. The findings show the need for continued observation as well as taking into account the treatment of other patients throughout different periods.

Key words: Progression free survival, Breast cancer, Overall survival, AC, EC, Taxanes, Combined Military Hospital (CMH).

Introduction

Breast cancer which accounts for 25% of all cancer diagnoses (1.68 million) and 15% of all cancer deaths (5,20,000) globally, is the most prevalent cancer in women and the leading cause of cancer death¹. One of the most fatal cancers for women worldwide remains breast cancer. In South Asia, it is the leading cause of cancer and cancer-related mortality in women². As per extrapolation, Bangladesh is likely to see a similar upward trend in breast cancer incidence and mortality as India (where the incidence of cancer is 25.8 per 1,00,000 women)³. Statistics from the cancer registry of the National Institute of Cancer Research & Hospital in Dhaka show a rise in the breast cancer rate, from 26.4 percent in 2008 to 30.1 percent in 2017⁴. Breast cancer has the greatest frequency of any type of cancer among Bangladeshi women between the ages of 15 and 44, with a rate of 19.3 per 1,00,000⁵. In cancers with hormone receptor-positive or negative features, chemotherapy has proven to be the most effective first-line treatment⁶. Chemotherapeutic agents including anthracyclines and taxanes are frequently utilized in the adjuvant and neoadjuvant treatment of early breast cancer. Usually, anthracycline-based chemotherapy is administered first, then a taxane in the treatment of early breast cancer⁷. This trial aimed to compare and evaluate the efficacy, feasibility, safety and three-year recurrence-free survival and three-year overall survival of the commonly used chemotherapy regimen AC followed by paclitaxel, AC followed by docetaxel, EC followed by paclitaxel, EC followed by docetaxel in cancer patients of Combined Military Hospital (CMH), Dhaka with previously untreated non-metastasis breast cancer.

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Materials and Methods

Patients with non-metastatic breast cancer on standard chemotherapy treatment administered after or before surgery were enrolled in a single-center, randomized, retrospective study. The investigation was carried out in the Department of Medical Oncology at CMH, Dhaka. The institutional review board of the partnering hospital gave its approval to the study protocol. After giving informed consent, patients were randomized into therapy groups. A total of 102 breast cancer patients aged 31 to 74 were randomly assigned to the study from June 2016 to January 2020. This study compared three-year survival and progression-free survival among four standard chemotherapy regimens. Fifty-six patients (54.9%) were treated with the chemotherapy regimen AC followed by paclitaxel and 13 patients (12.75%) were treated by AC followed by docetaxel. Twenty-one patients (20.59%) were treated with EC followed by paclitaxel whereas 12 patients (11.76%) were treated by EC followed by docetaxel. Surgery, chemotherapy and radiation therapy are the initial lines

of treatment in this study. Patients who objected to receiving postoperative adjuvant therapies were not included in this study. Since they had previously been rejected from clinical trials and active treatment plans, patients beyond the age of 75 were also not allowed to participate in this study.

Results

Among all the patients, 22(21%) patients had cancer in their family history. The consumption rate of betel leaf (53%) was significantly higher than smoking (3%). Two percent of the patients consumed alcohol when compared to other habits (14%). None of the habits was observed in 42% of the patients.

Table-I: Self-report verified by medical record review (n=102)

Name of comorbidities	Percentage (%)
Hypertension	34
DM	21
COPD	28
CKD	18
None	31

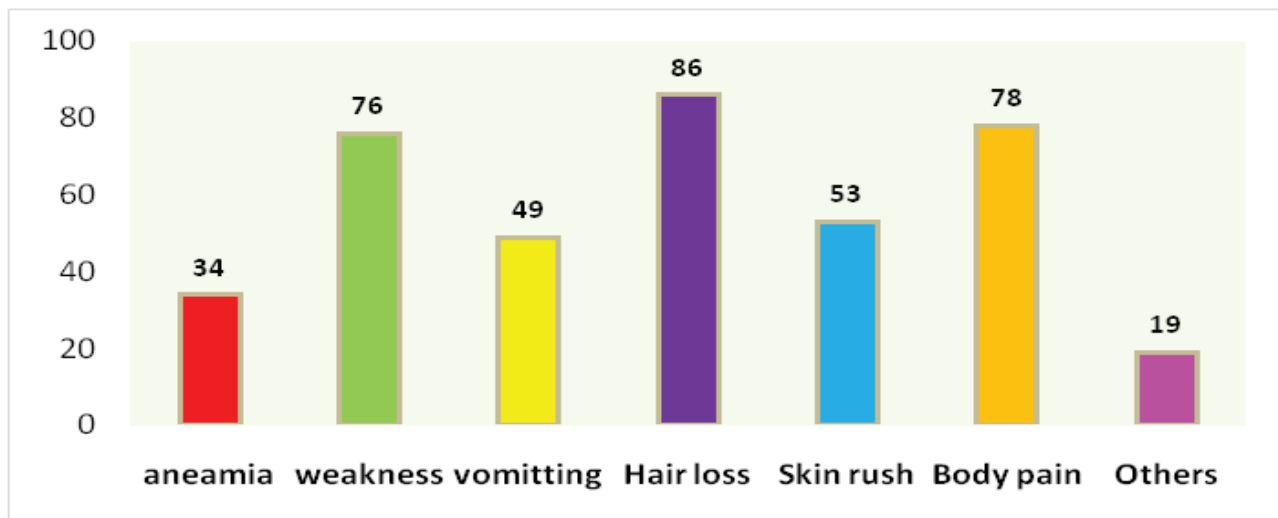


Figure-1: Side effects associated with chemotherapeutics

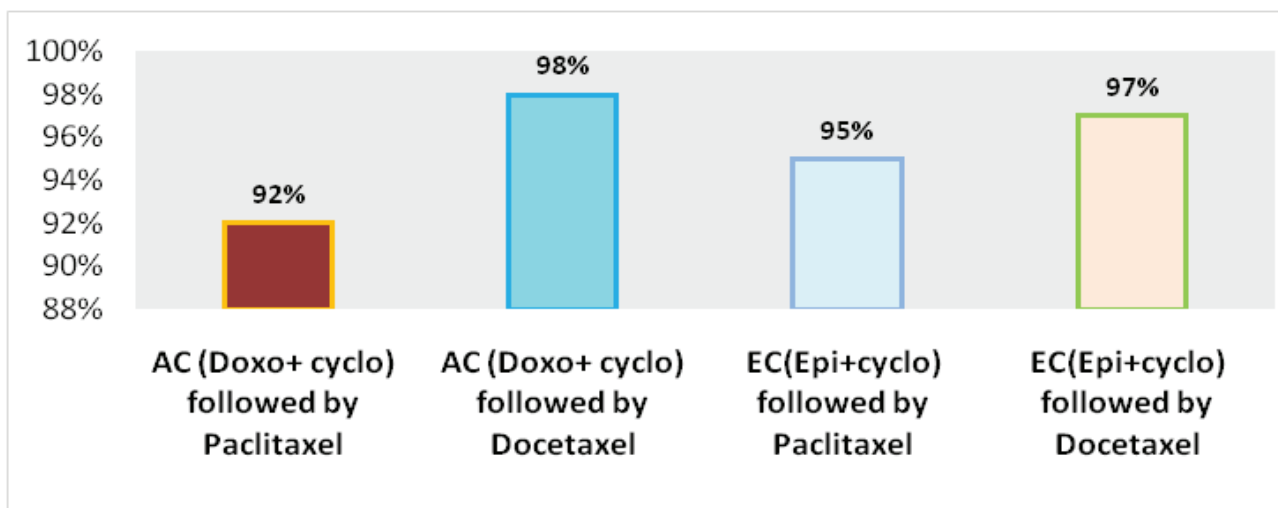


Figure-2: Three years' OS among chemotherapy regimens

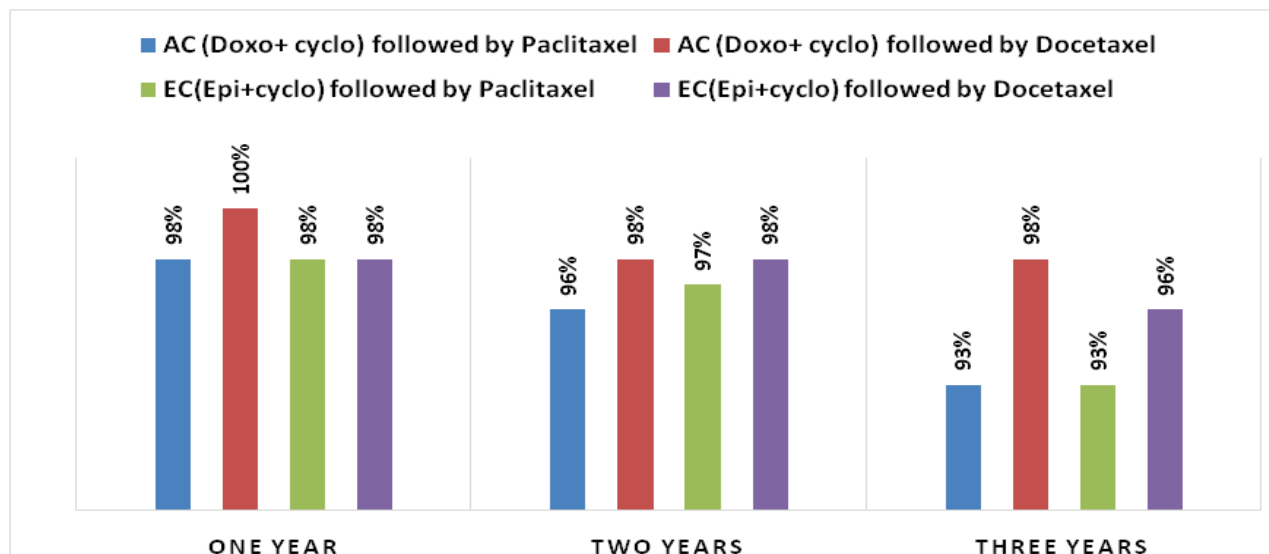


Figure-3: PFS rate among chemotherapy regimens

During the investigation, patients self-reported their comorbidities which was confirmed by reviewing the medical records (Table-I). More than one third (34%) of the participants reported hypertension. COPD was denoted as the second (28%) most prevalent comorbidity among the population. Participants disclosed comorbidities like DM (21%) and CKD (18%). No sign of comorbidities was observed in 31% of the study population.

As side effects of chemotherapy, a significant portion of the population showed the symptoms of hair loss (86%), body pain (78%) and weakness (76%). Almost half of the population suffered from skin rash (53%) and vomiting (49%) while the sign of anaemia was found in 34% of the patients. Nineteen percent of the population suffered from other side effects like loss of appetite, tiredness and nausea (Figure-1).

Sixty-seven percent of patients completed 15 fractions radiotherapy but 33% of the patients did not receive any radiotherapy treatments. According to the guidelines, 21 patients did not need chemotherapy for their treatment. But 12 patients didn't receive radiotherapy because of various economical and other reasons. Seventy-one (69.61%) patients received adjuvant chemotherapy and thirty-one (30.39%) patients received neoadjuvant chemotherapy. Figure-2 represents OS after three years was 92% in AC followed by paclitaxel, 98% in AC followed by docetaxel and 95% and 97% in EC followed by paclitaxel and docetaxel respectively. One year of PFS in AC followed by paclitaxel and docetaxel was 98% and 100% respectively and EC followed by paclitaxel and docetaxel were 98% and 98%. Two years of PFS among four regimens 96%, 98%, 97% and 96% respectively. This study also finds three-year survival among four chemotherapy regimens 93%, 98%, 93% and 96% respectively which is represented in Figure-3.

Discussion

Patients without comorbidities survive longer than those with comorbidities⁸. In this study, the five common comorbid illnesses were hypertension (34%), COPD (28%), diabetes (21%) and chronic kidney disease (18%). Lack of physical activity, inappropriate nutrition intake, excessive alcohol consumption, tobacco use and obesity are the common risk factors that diabetes and cardiovascular disease share with breast cancer⁹. In this study, history of consumption of betel leaf was found significantly high.

Chemotherapy's side effects have an impact on a person's physical health, quality of life and emotional state. Hair loss was found as a profound (86%) side effect of chemotherapeutics in this investigation. When hair loss totals more than 150 per day, it is deemed abnormal. Chemotherapy-induced hair loss is a treatable disorder known as alopecia. Paclitaxel and docetaxel are two of the most potent hair loss inducers, mainly due to a mechanism that causes dystrophic anagen effluvium¹⁰. After initiating the chemotherapy, chemotherapy-induced hair loss develops subacutely rapidly before turning severe after a few weeks. Following chemotherapy, hair growth will often return in a regular pattern after three months and reaches a pleasant appearance six months later¹¹. The pain was noted as one of the most prevalent adverse effects that might occur as a result of the disease or medication throughout this study. The feeling of tiredness can be triggered by anaemia, sleep disturbances, inadequate nutrition, metabolic problems or an inflammatory reaction and can last from six months to two years after remission¹². Cancer-related anaemia is caused by malignant cells infiltrating the bone marrow, reduced haemoglobin synthesis due to therapy, iron shortage and low erythropoietin levels¹³.

OS the duration of patient survival from the time of treatment initiation, is a universally-accepted direct measure of clinical benefit¹⁴. OS of doxorubicin and cyclophosphamide followed by docetaxel arm is better than the other three arms but one limitation may affect these results. The size of the population number in this study is not equal to four arms which can influence the results. The interval between therapy beginning and tumour development or death from any cause is defined PFS¹⁵. PFS and OS will be linked by design, as OS is made up of PFS plus post-progression survival¹⁶.

Conclusion

AC or EC followed by taxane regimens well suitable regimens for the population of patients with previously untreated non-metastatic breast cancer patients. The findings show the need for continued observation as well as taking into account the treatment of other patients throughout different periods.

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