ORIGINAL RESEARCH

Echocardiographic Evaluation of Breast Cancer Patients on Chemotherapy

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ABSTRACT

Background: Cardiovascular disease in patients with breast cancer undergoing chemotherapy is of major growing concern. The commonly used chemotherapeutic regimen have cardiotoxic effects including doxorubicin, trastuzumab and other agents .these have acute effects on cardiac function and longterm effects on cardiac remodelling and function. There have been a few studies on this regard, Hence we aimed to investigate the early effects of chemotherapy on cardiac function in addition to association of N – terminal pro-brain natriuretic peptide and echocardiagraphic indices.

Methods: This is a prospective, single-center study including 100 patients who received a breast cancer diagnosis in the Government Royapettah Hospital between July 2021 and April 2022 before beginning chemotherapy. Before beginning chemotherapy (baseline -T1), the day following the conclusion of the second cycle (T2), and the day following the conclusion of the fourth cycle (T3), 2D echocardiography was performed on all patients enrolled.

Results: It showed that the mean age of the subjects was 44.2 ± 8.80 years. Out of all the subjects, 40% had breast cancer of right side and 60% had breast cancer of left side. Thirty percent subjects had diabetes and 40% had hypertension. Maximum subjects had undergone surgery (70%). The chemotherapy regimen followed in most of the subjects was ACP-regimen in 70% subjects, followed by 20% having CMF- regimen and 10% having TCH-regimen. It was seen that out of all the variables, only TAPSE, and S'–TV have significant difference at T1, T2 and T3. In our study 20 % had LV systolic dysfunction, 20% had LV diastolic dysfunction and 30% had RV systolic dysfunction which correlate with NT pro BNP values.

Conclusion: Tissue Doppler echocardiography is currently used and is sufficient for providing chemotherapy patients with effective cardiac care in places with limited resources. Our study also enlighten that Echo should performed at T1 and T3 stage for all chemotherapy patients with focus on RV function as it is the earlier marker for cardiotoxicity. Future molecular mechanisms will facilitate the use of medications that operate on certain molecular targets to treat cardiotoxicity

Keywords: Chemotherapy, Echocardiography, Heart, TAPSE

INTRODUCTION

The common malignancy among women is breast cancer [1, 2]. The last 15 to 20 years have seen a dramatic improvement in breast cancer survival, largely because of advancements in cancer treatment [3]. Nevertheless, several anticancer medications used to treat breast cancer patients have the potential to cause cardiac damage (cardiotoxicity).Early and late cardiotoxicity is a side effect of chemotherapy regimens containing anthracyclines,

cyclophosphamide, fluorouracil, cisplatin, taxanes, and trastuzumab [4]. Cardiomyopathy with or without overt congestive heart failure is included in the list of cardiotoxicity caused by chemotherapy. A possible early sign of chemotherapy-induced heart injury is impaired diastolic cardiac function [5]. Recently, a valuable technique for earlier detection of local anomalies in cardiac functions before the heart is affected has been tissue Doppler echocardiography (TDI), which permits assessment of systolic and diastolic velocities of ventricular walls [6,7].Despite extensive research on the left ventricular diastolic and systolic functions following chemotherapy, little is known about the right ventricular functions, whose prognostic significance rises in the presence of left ventricular systolic dysfunction [8]. Its crescentic anatomical and morphological form makes echocardiographic assessment challenging. The right ventricle is functionally and physically separated into inflow and outflow tracts [9]. Right heart evaluation can be done using M-mode echocardiography, two-dimensional echocardiography, conventional Doppler echocardiography, and myocardial Doppler tissue imaging, especially when utilised in conjunction [10].In patients with breast cancer who got anthracycline, cyclophosphamide, and 5-fluorouracil (5-FU) and were receiving chemotherapeutics for the first time in their life, we looked into any early effects of cancer chemotherapy on the right heart in a relatively short amount of time. Additionally, we looked for a connection between the right heart echocardiographic indices and blood levels of N-terminal pro-brain natriuretic peptide (NT-proBNP), a well-known measure of cardiac injury that has been found to predict subtly damaged myocardium in chemotherapy survivors [11,12].

METHODS

This is a prospective, single-center study including 100 patients who received a breast cancer diagnosis in the Government Royapettah Hospital between July 2021 and April 2022 before beginning chemotherapy. Before beginning chemotherapy (baseline -T1), the day following the conclusion of the second cycle (T2), and the day following the conclusion of the fourth cycle (T3), 2D echocardiography was performed on all patients enrolled. A skilled cardiologist performed the 2d echocardiography, and the results were verified by a second cardiologist who was doubly blinded to the study.Those who were diagnosed with breast cancer before to beginning chemotherapy, those underwent breast cancer surgery prior to beginning chemotherapy, or those underwent radiotherapy prior to chemotherapy were included in the study. Exclusion criteria include: those who have previously undergone chemotherapy; those who have moderate to severe left ventricular dysfunction; those who are ill and are not candidates for chemotherapy; and those who have not given consent for the study.Three common Chemotherapy regimens were used .1.ACP(70%)- Adriamycin 60 Mg/M2Cyclophosphamide 600 Mg /M2, Paclitaxel 175mg/ M2 . 2. CMF(20%) - Cyclophosphamide 100mg/m2 Methotrexate 40mg/m25FU600mg/m2, 3. TCH (10%)- Taxale (Docetaxel) 75 mg/m2 C - carboplatin 6mg/kg H – herceptin (Traztuzumab6-8 mg/kg)Software known as Statistical Package for Social Sciences (SPSS) version 23 was used for data analysis (SPSS Inc., Chicago, IL, USA). First, parametric test conditions were examined for the continuous variables. To ascertain if the continuous variables were normally distributed, the Shapiro-Wilk test was employed. Where appropriate, descriptive data were displayed as mean standard deviation or median (minimum - maximum). The Friedman test was used to assess median differences rather than mean differences between measurement times, which were compared using repeated measures of ANOVA. Which measurement time varies from which others was determined using the Bonferroni's adjusted multiple comparison test or the Bonferroni's adjusted Wilcoxon's sign-rank test where the P-values from the ANOVA or Friedman's test statistics were statistically significant. By using

Spearman's correlation analysis, degrees of relationship between continuous variables were calculated. Statistical significance was defined as a P-value < 0.05.

RESULTS

Variable (n=100)	
Age (in years) Mean ± SD	 44.2 ± 8.80
Breast Cancer Right Side Left Side	 40 60
Co morbidities Diabetes Hypertension	 30 40
Surgery Yes No	 30 70
Chemotherapy ACP- regimen CMF- regimen TCH- regimen	 70 20 10

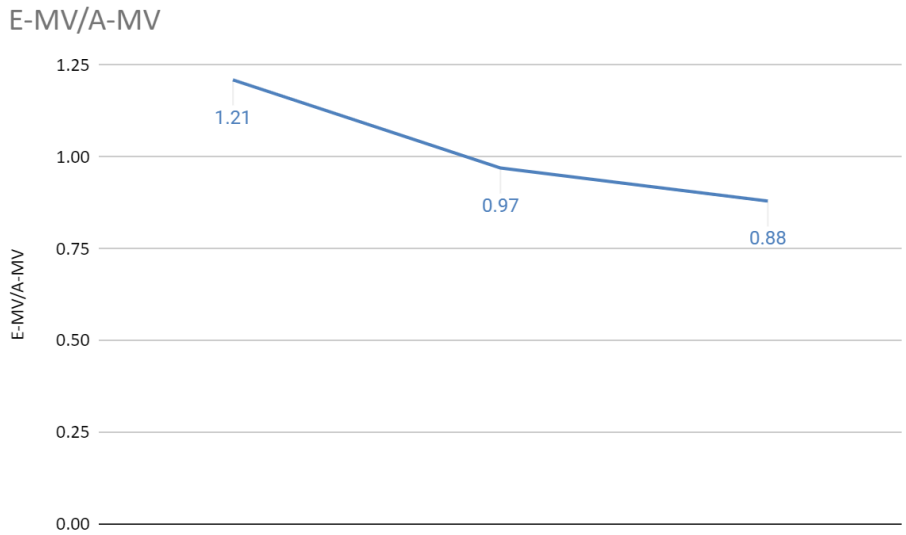
Table 1: Characteristics of study population

Table 1 depicted the characteristics of the study population. It showed that the mean age of the subjects was 44.2 ± 8.80 years. Out of all the subjects, 40% had breast cancer of right side and 60% had breast cancer on the left side. Thirty percent subjects had diabetes and 40% had hypertension. Maximum subjects had undergone surgery (70%). The chemotherapy regimen followed in most of the subjects was ACP- regimen in 70% subjects, followed by 20% having CMF- regimen and 10% having TCH-regimen.Table 2 showed the echocardiographic measurements of the study population at T1. T2, and T3. It was seen that out of all the variables, only TAPSE, and S'–TV have significant differences at T1, T2 and T3. This table showed that the LVEF (%) has a decreasing trend from T1 to T2 to T3. Out of all- 20% of the patients had LVEF below 50%, which decreased during T2. The LVID values showed an increasing trend. The mean difference between the T1, T2 and T3 was 1.65 ± 0.16 mm. TAPSE showed a decreasing trend with a mean difference of 1.25 ± 0.15 mm between T1, T2 and T3. 30% of the patients had TAPSE<16. The value of S'–TV has a decreasing trend with a mean difference of 1.05 ± 0.24 cm/s. Only 30% of patients showed S' value < 9.5. There was a decreasing trend seen in the values of E-MV/A-MV. Approximately 20% patients have E-MV/A-MV value <0.8 during T2 and T3. Both E-MV/E'-MV and E-TV/ E'-TV showed increasing trends during T1, T2 and T3.

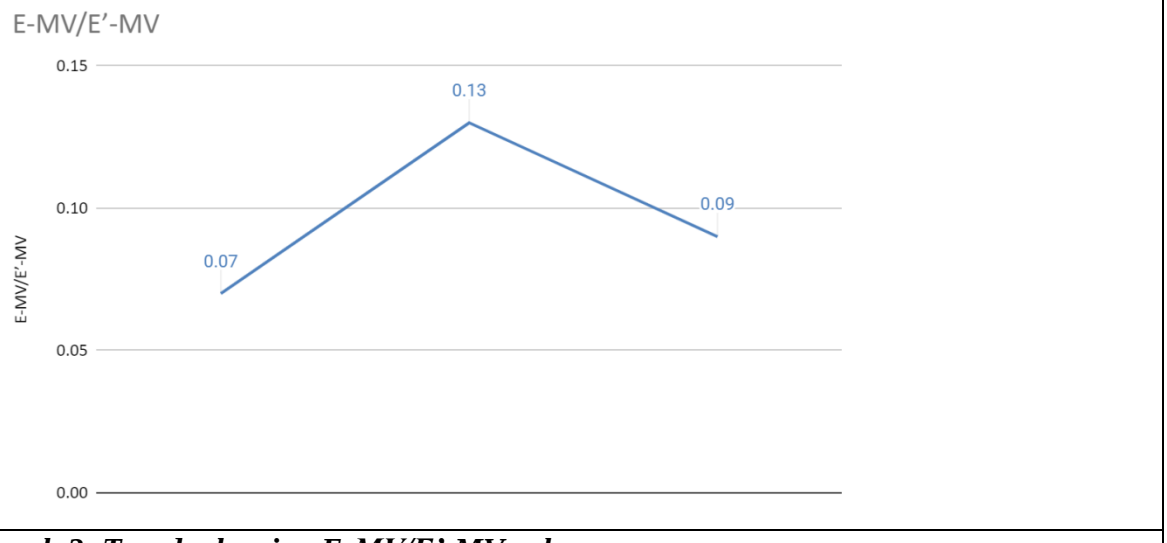
Variable (n=100)	**T1**	**T2**	**T3**	**F value**	**P value**
LVID (in mm)	40.8 ± 7.50	42.6 ± 7.30	44.1 ± 7.17	0.81	0.61
LVIS (in mm)	27.4 ± 6.08	29.3 ± 5.85	30.9 ±6.55	0.81	0.46
LVEF (in %)	61.3 ± 5.9	58.9 ± 6.71	57.1 ± 6.79	1.06	0.36
E-MV (in cm/s)	0.73 ± 0.22	0.73 ± 0.22	0.71 ± 0.20	0.03	0.97
A-MV (in cm/s)	0.62 ± 0.17	0.78 ± 0.22	0.85 ± 0.27	2.78	0.08
E'-MV (in cm/s)	10.2 ± 1.87	8.8 ± 1.72	8 ± 1.73	3.94	0.03
TAPSE (in mm)	21.7 ±1.27	20.7 ±1.19	19.2 ± 1.4	9.52	0.0007
E-TV (in cm/s)	0.57 ± 0.13	0.57 ± 0.13	0.57 ± 0.13	0	1
A-TV (in cm/s)	0.49 ± 0.18	0.58 ± 0.16	0.67 ± 0.17	2.80	0.08

E'- TV (in cm/s)	11.1 ± 1.92	10.4 ± 2.01	9.4 ± 1.85	1.96	0.16
S'–TV (in cm/s)	12.9 ± 1.04	12 ± 1.41	10.9 ± 1.3	6.32	0.005
TRPG (in mm Hg)	14.7 ± 3.07	16.6 ± 4.10	19.1 ± 6.59	2.10	0.14
PASP (in mm Hg)	19.7 ± 3.07	22.1 ± 4.18	24.6 ± 6.37	2.67	0.09
E-MV/A-MV	1.21 ± 0.28	0.97 ± 0.27	0.88 ± 0.27	3.89	0.03
E-MV/E'-MV	0.07 ± 0.02	0.13 ± 0.12	0.09 ± 0.02	1.84	0.17
E-TV/ E'-TV	0.05 ± 0.009	0.06 ± 0.009	0.06 ± 0.10	0.09	0.91
E-TV/ A-TV	1.23 ± 0.32	1.03 ± 0.31	0.88 ± 0.26	3.48	0.04

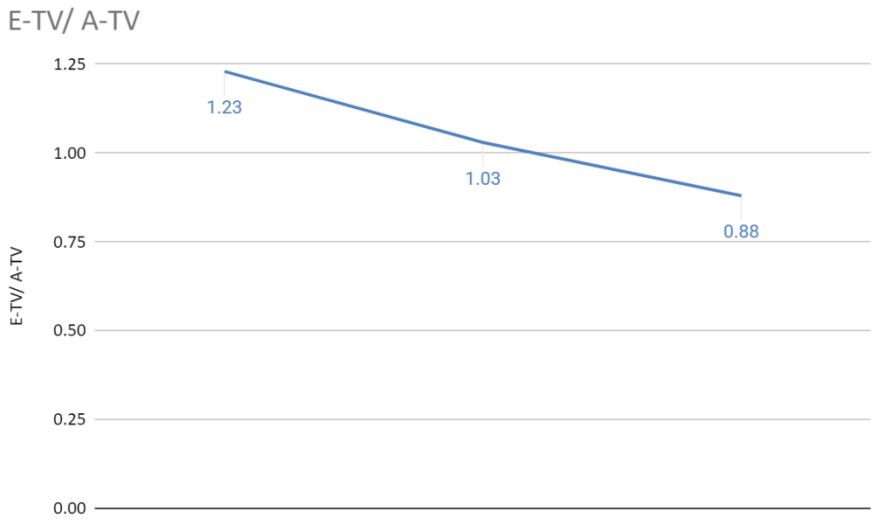
Table 2: Echocardiography Measurements of Study Population



Graph 1: Trends showing E-MV/A-MV values



Graph 2: Trends showing E-MV/E'-MV values



Graph 3: Trends showing E-TV/A-TV values

DISCUSSION

While most echocardiographic indices remain within the normal range and do not result in any clinical signs of right heart failure, we have shown that chemotherapeutic medicines reduce right ventricular systolic and diastolic functions in a reasonably short amount of time. After the first dose of the medication was infused, some TDI indexes experienced an immediate reduction. Additionally, it was discovered that the decline TAPSE following two cycles of chemotherapy was connected with a rise in serum NT-proBNP concentrations. Subclinical cardiac damage has been documented in multiple trials, usually involving anthracyclines [13], and in particular, diastolic impairment in the left ventricle has been shown to precede systolic derangement [14 -16]. In numerous papers [17, 18], TDI has been recommended as the preferred approach to identify early cardiac damage brought on by cancer chemotherapy. However, it has recently been discovered that myocardial deformation parameters (strain and strain rate) can identify subclinical myocardial injury earlier than myocardial velocity measurements [19]. After three cycles of pegylated doxorubicin treatment administered every three weeks and after six cycles of the same regimen, Jurcut et al. [20] found a significant reduction in both longitudinal and radial strain and strain rates. Subclinical systolic and diastolic cardiac anomalies were shown to persist up to 6 years of follow-up in research that combined TDI with speckle-tracking echocardiography [21]. In our study 20 % had LV systolic dysfunction, 20% had LV diastolic dysfunction and 30% had RV systolic dysfunction which correlate with NT pro BNP values.

CONCLUSION

Although there hasn't been any clinical worsening as a result of the echocardiographic indices being impaired after chemotherapy in a relatively short period of time, we have shown this. This study may draw attention to heart in cancer patients and pave the way for larger studies that examine the potential link between short-term variations in heart echocardiographic indices and long-term prognosis. Early detection and treatment of cancer due to molecular advances improve the overall prognosis of cancer patients. However, new research indicates that all chemotherapy patients should undergo early echocardiographic testing and follow-up care due to the cardiotoxicity of chemotherapeutic drugs. According to this study, early detection of heart damage and a change in the patient's chemotherapeutic regimen will improve the care and prognosis of breast cancer patients. To improve the overall cardiac

treatment of oncology patients, we must create a dedicated cardio-oncology team that will utilise future multimodality imaging technologies like cardiac MRI and LV strain imaging. Tissue Doppler echocardiography is currently used and is sufficient for providing chemotherapy patients with effective cardiac care in places with limited resources. Future molecular mechanisms will facilitate the use of medications that operate on certain molecular targets to treat cardiotoxicity. Recently 1st Cardiooncology Guideline is published in ESC 2022 and it highlights the timing of Echocardiography and approach in chemotherapeutic patients. Our study also enlighten that Echo should performed at T1 and T3 stage for all chemotherapy patients with focus on RV function as it is the earlier marker for cardiotoxicity

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