ECG changes as Cardiac Toxicity of Concurrent Trustuzumab and Paclitaxel in Adjuvant Treatment of HER-2 positive Breast Cancer

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Abstract

Background: Breast cancer accounts for 10% of US female cancer cases and second in worldwide cancer fatalities. Overexpression of the ERBB2 oncogene in 20-25% of invasive breast tumors implies aggression. Trastuzumab improves outcomes via HER2. HER2-targeted chemotherapy with albumin-paclitaxel and Trastuzumab is used increasing survivability but may induce cardiotoxicity by blocking HER2. It works with chemotherapy for HER-2/neu positive breast cancer.

Objectives: To evaluate Cardiac toxicity of concurrent Trustuzumab and Paclitaxel in Adjuvant treatment of HER-2 positive Breast Cancer

Patients and methods: This was prospective hospital-based study at Qena University Hospital, with 30 participants post-radical surgery and anthracycline-based chemotherapy for unilateral ductal carcinoma, HER2-positive. Physical exams, lab tests, ECG, and Echo was done. Adjuvant trastuzumab administered with paclitaxel for 4 cycles, then continued for 1 year.

Results: Age >55 (50%), obesity (43.3%), hypertension, hyperlipidemia (30%), diabetes (16.7%). Electrocardiogram (ECG) abnormalities increased after 4 cycles (16.7%), 6 months (23.3%), 9 months (33.3%), and 12 months with trastuzumab monotherapy (53.3%). ECG abnormalities were more common in trastuzumab monotherapy (46.7%) than in Paclitaxel (16.7%). P-wave, ST-segment, T-wave, and QRS changes were notable. Trastuzumab treatment increased T-wave alterations (20% vs. 0% baseline) and arrhythmias (33.3% vs. 3.3% baseline) after 12 months, but Paclitaxel did not (16.7% vs. 3.3% after 4 cycles). There was statistically significant decline in LVEF%, MAPSE, TAPSE, E/E and RV FAC and significant increase in LVESD, LVEDD, LVISD, LA, E/A after treatment by trastuzumab alone.

Conclusion: LVEF% was significantly higher after 12 months of trastuzumab alone however, more patients developed ECG abnormalities.

Keywords: Cardiac toxicity; Trustuzumab; Paclitaxel; HER-2; Breast Cancer.

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Introduction

Breast cancer is the most prevalent female cancer in the United States, constituting over 10% of new cancer diagnoses annually and ranking as the second leading cause of cancer-related death in women globally **(Singh et al., 2023; DeSantis et al., 2019).**

Amplification or overexpression of the ERBB2 oncogene (HER2 or HER2/neu) is found in approximately 20-25% of primary invasive breast cancers, correlating with an aggressive natural history and diminished overall survival **(Asgari-Karchekani et al., 2022).** Patients diagnosed with all stages of HER2-positive breast cancer have experienced significant improvement in outcomes due to the approval of therapies specifically targeting HER2 **(Goutsouliak et al., 2020).** Current treatment for HER2-positive breast cancer primarily involves chemotherapy combined with HER2-targeted therapy, with the albumin-paclitaxel and Trastuzumab combination being a prevalent and effective regimen **(Wang et al., 2022).**

Trastuzumab, a humanized monoclonal antibody against the extracellular domain of HER2, has enhanced disease-free and overall survival. However, it is associated with cardiotoxicity, leading to an asymptomatic decline in left ventricular ejection fraction or symptomatic heart failure **(Guan et al., 2021).** The mechanism behind trastuzumab-induced left ventricular systolic dysfunction is linked to the blockade of HER2 signaling, disrupting the normal stress response and cellular repair mechanisms of cardiomyocytes **(Ebrahim et al., 2022).** Trastuzumab exhibits moderate activity as a single agent but demonstrates high efficacy when combined with chemotherapy as a front-line therapy in HER-2/neu positive breast cancer **(Yamashita et al., 2021).**

The main aim of this study was to evaluate Cardiac toxicity of concurrent Trustuzumab and Paclitaxel in Adjuvant treatment of HER-2 positive Breast Cancer.

Patients and Methods

This investigation is characterized as a prospective hospital-based study conducted at the Clinical Oncology Department of Qena University Hospital in Qena, Egypt under Ethical Code: **SVU-MED-ONM027-CLO027-2-21-8-228**. The study population consists of thirty individuals who have undergone radical surgery and received anthracycline-based chemotherapy, are over 25 years old, and have histologically confirmed unilateral ductal carcinoma of the breast without distant metastasis or concurrent malignancies. Additionally, participants must exhibit normal cardiac, renal, and pulmonary functions.

Inclusion criteria

- Age (25-65) years.
- Pathology proven breast cancer with positive her 2 neu receptor.
- Patients who didn't receive AC regimen previously.

Exclusion criteria

- Age <25 and >65 years.
- Cardiac patient.

Methods

The methodology involved a thorough examination of patients, gathering information on personal history (demographics, habits, especially smoking), reproductive history (menstrual details, pregnancies, hormonal therapies), drug sensitivity, and medical history (cardiac, hypertension, chest, renal, liver, blood diseases). Detailed documentation of breast symptoms, past surgeries, and family history, specifically breast or ovarian cancer in first-degree relatives, was integral to the investigation, with additional consideration for other family cancers.

Patient characterization involved recording age and sex, tumor size, histopathological features, and the status of K167 and hormonal receptors.

Physical exams included several topics. General appearance for distress, cachexia, or pallor, breast symmetry, skin changes (redness, dimpling, swelling), nipple changes (inversion, discharge), and areola changes were assessed. General examination also included weight measurement, systolic and diastolic blood pressure were measured, and the heart rate was also measured. Palpation revealed breast tissue abnormalities, axillary, supraclavicular, and infraclavicular lymph node enlargement or pain, chest wall masses, and nipple inversion or discharge. Skin and tissue changes like dimpling or puckering (peau d'orange) and redness or edema may indicate underlying concerns. Palpable axillary lymph node enlargement may signal lymph node cancer spread.

Electrocardiography (ECG) during trastuzumab administration involved monitoring specific criteria for cardiac toxicity. Criteria included evaluating the QT interval for potential prolongation, with a prolonged QT interval associated with an elevated risk of ventricular arrhythmias. Measurement involved assessing the QT interval from the onset of the QRS complex to the end of the T wave, often corrected as QTc to accommodate heart rate variations. Additionally, criteria for cardiac toxicity encompassed observing ST-segment changes indicative of myocardial ischemia or injury, T-wave changes such as flattening, inversion, or altered morphology, and the development of new or worsening arrhythmias. Monitoring involved vigilance for irregularities in rhythm, such as premature beats, atrial fibrillation, or ventricular tachycardia. Furthermore, criteria included identifying bradyarrhythmias such as sinus bradycardia or heart block, suggesting potential conduction system abnormalities, as well as the presence of U waves after T waves, which may suggest hypokalemia. Abnormal Q waves were also considered as they could indicate a previous myocardial infarction.

Echocardiography (Echo): transthoracic echocardiography was performed with a 1.5–3.6 MHz multi-frequency phased array probe. The 2-dimensional (2D) echocardiography were used to measure the left ventricular (LV) end systolic diameter (LVESD), end diastolic diameter (LVEDD), while the M-mode was used for EF after measuring the LVEDD, LVESD. Tricuspid annular plane systolic excursion (TAPSE), measured as the displacement of the tricuspid lateral annulus between systole and diastole, and the Mitral Annular Plane Systolic Excursion (MAPSE) were recorded in M-mode. The LA volume at the time just before mitral valve opening on the apical 4- and 2-chamber views was determined offline using Simpson's biplane disc summation method. Pulsed wave (PW) Doppler study was performed in the apical 4 chamber view within 3 mm sample volume at the tip of the mitral leaflets to obtain mitral inflow velocities to assess LV filling. Using PW Doppler; the peak E (early diastolic) wave velocity, A (late diastolic) wave velocity, and the early (E) mitral inflow velocity to early (E) mitral annular velocity was recorded, then ratio of E/A and E/E were calculated. Pulsed wave (PW) Doppler was also used to assess the Left Ventricular Posterior Wall thickness at end-diastole (LVPWD). Other measured parameters included Interventricular Septum thickness at end-diastole (IVSd), Left Ventricular Posterior Wall thickness at end-diastole (LVPWd) and Right Ventricular Fractional Area Change (RVFAC).

The procedures involved administering adjuvant trastuzumab therapy (8mg/kg during the first cycle then 6 mg/m^2 rest of the cycles) with 4 cycles of paclitaxel (80 mg/m^2), followed by a total duration of 1 year of trastuzumab therapy (6 mg/m^2).

Statistical analysis

IBM SPSS version 22.0 was used to analyses computer-generated data. To express quantitative data, percentages and numbers were employed. Chi-Square adjustment was applied to tables demonstrating non continuous data and t.test for continuous data.

Results

This study included 30 subjects who received trastuzumab and Paclitaxel adjuvant treatment for HER-2 positive breast cancer, their age ranged between 43-61 yeas with mean value of 54.4±4.89. the tumor size age ranged between 2.8-5.9 cm with mean value of 4.16±0.84. the majority of them 80% were invasive ductal carcinoma and 20% were invasive lobular carcinoma. The tumor was right sided in 53.3%. Estrogen receptors were detected in 66.7% of patients, Progesterone receptor were detected in 60% of patients. Ki67 level ranged between 7-34 with mean value of 14.6±9.01, (**Table.1).**

Table 1. Participating subjects Characteristics

Variables		N=30
Age (year)	**Range (median)**	43-61 (54.5)
	Mean ± SD	54.4±4.89
Tumor size	**Range (median)**	2.8-5.9 (3.9)
	Mean ± SD	4.16±0.84
Side	**Right breast**	16 (53.3%)
	Left breast	14 (46.7%)
Histopathology	**invasive ductal carcinoma**	24 (80%)
	invasive lobular carcinoma	6 (20%)
Stage	**1A**	11 (36.7%)
	2A	10 (33.3%)
	2B	6 (20%)
	3A	3 (10%)
Estrogen receptor	**Yes**	20 (66.7%)
	NO	10 (33.3%)
Progesterone receptor	**Yes**	18 (60%)
	No	12 (40%)
Ki-67 (protein)	**Range (median)**	7-34 (10)
	Mean ± SD	14.6±9.01

The study examined various cardiac risk factors in the participating subjects. Among these factors, individuals aged over 55 years constituted 50% of the cohort, while 43.30% were identified as obese. Additionally, 30% of the subjects had hypertension (HTN), and an equal percentage exhibited hyperlipidemia. Diabetes mellitus (DM) was found in 16.70% of the participants (**Fig.1).**

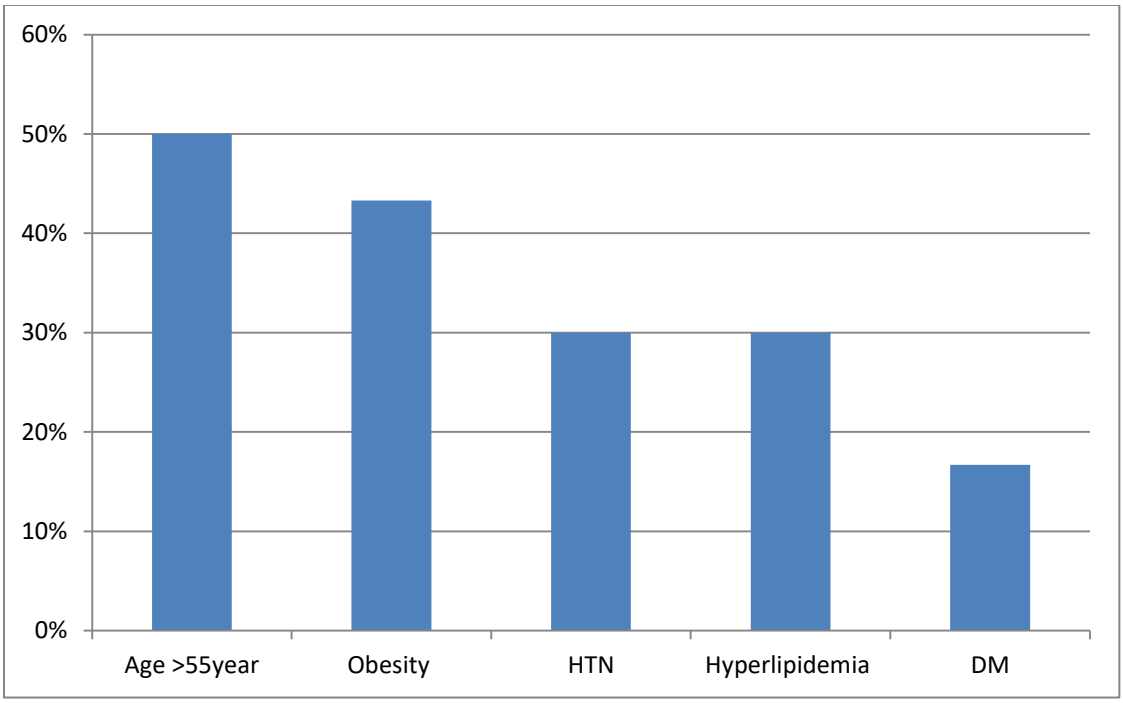

Fig.1. Cardiac risk factors among participating subjects.

The incidence of ECG abnormalities increased over time: after 4 cycles, 16.7%, after 6 months, 23.3%, after 9 months, 33.3%, and after 12 months (with trastuzumab alone), 53.3%. Comparatively, trastuzumab alone led to a significantly higher rate of ECG abnormalities (46.7%) than when combined with Paclitaxel (16.7%). Specific ECG changes included P-wave, ST-segment, T-wave, and QRS changes. Notably, T-wave changes were significantly higher after 12 months of trastuzumab alone (20% vs 0% at baseline). Additionally, arrhythmias increased over time with trastuzumab alone, reaching 33.3% after 12 months, compared to 3.3% at baseline. In contrast, the difference in arrhythmias after 4 cycles of trastuzumab and Paclitaxel adjuvant treatment and baseline was statistically insignificant (16.7% vs 3.3%), (**Table.2 & Fig.2,3).**

Table 2. Comparison of ECG before and after chemotherapy in participating subjects

Variables	**Baseline**	**After 4 cycles trastuzumab and Paclitaxel adjuvant ttt**	**After 6 months trastuzumab alone**	**After 9 months trastuzumab alone**	**After 12 months trastuzumab alone**	**Baseline vs after adjuventtrastuzumab& Paclitaxel**	**Baseline vs trastuzumab alone**
	N=30	***N=30***	***N=30***	***N=30***	***N=30***		
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**p-value**	**p-value**
Abnormalities							
Yes	0 (0%)	5 (16.7%)	7 (23.3%)	10 (33.3%)	14 (46.7%)	0.020	0.00001*
No	30 (100%)	25 (83.3%)	23 (76.7%)	20 (66.7%)	16 (53.3%)		

ECG Findings							
P-wave changes	0 (0%)	1 (3.3%)	2 (6.7%)	3 (10%)	3 (10%)	0.313	0.403
ST- segment changes	0 (0%)	3 (10%)	4 (13.3%)	5 (16.7%)	5 (16.7%)	0.075	0.086
T-wave changes	0 (0%)	1 (3.3%)	3 (10%)	6 (20%)	6 (20%)	0.313	0.029*
QRS changes	0 (0%)	1 (3.3%)	3 (10%)	4 (13.3%)	4 (13.3%)	0.313	0.201
Cardiac arrhythmia							
SVT	0 (0%)	1 (3.3%)	2 (6.7%)	3 (10%)	3 (10%)	0.878	0.998
Sinus tachyarrhythmia	1 (3.3%)	2 (6.7%)	3 (10%)	4 (13.3%)	4 (13.3%)		
Ventricular premature beats	0 (0%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)		
First-degree AVB	0 (0%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)		
Intraventricular block	0 (0%)	0 (0%)	1 (3.3%)	1 (3.3%)	1 (3.3%)		
Total	1 (3.3%)	5 (16.7%)	8 (26.7%)	10 (33.3%)	10 (33.3%)	0.085	0.024*

Supraventricular tachycardia (SVT), atrioventricular Block (AVB), *significant

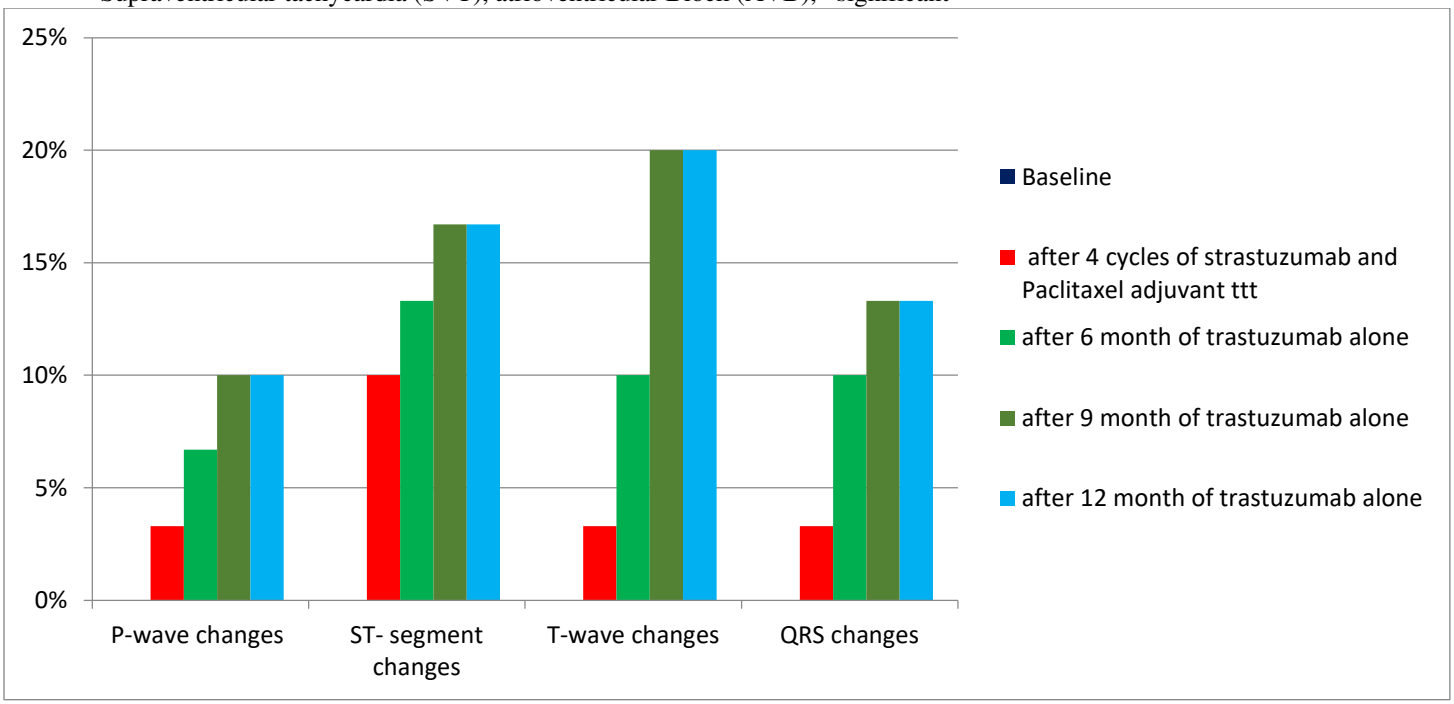

Fig.2. ECG changes before and after chemotherapy in participating subject.

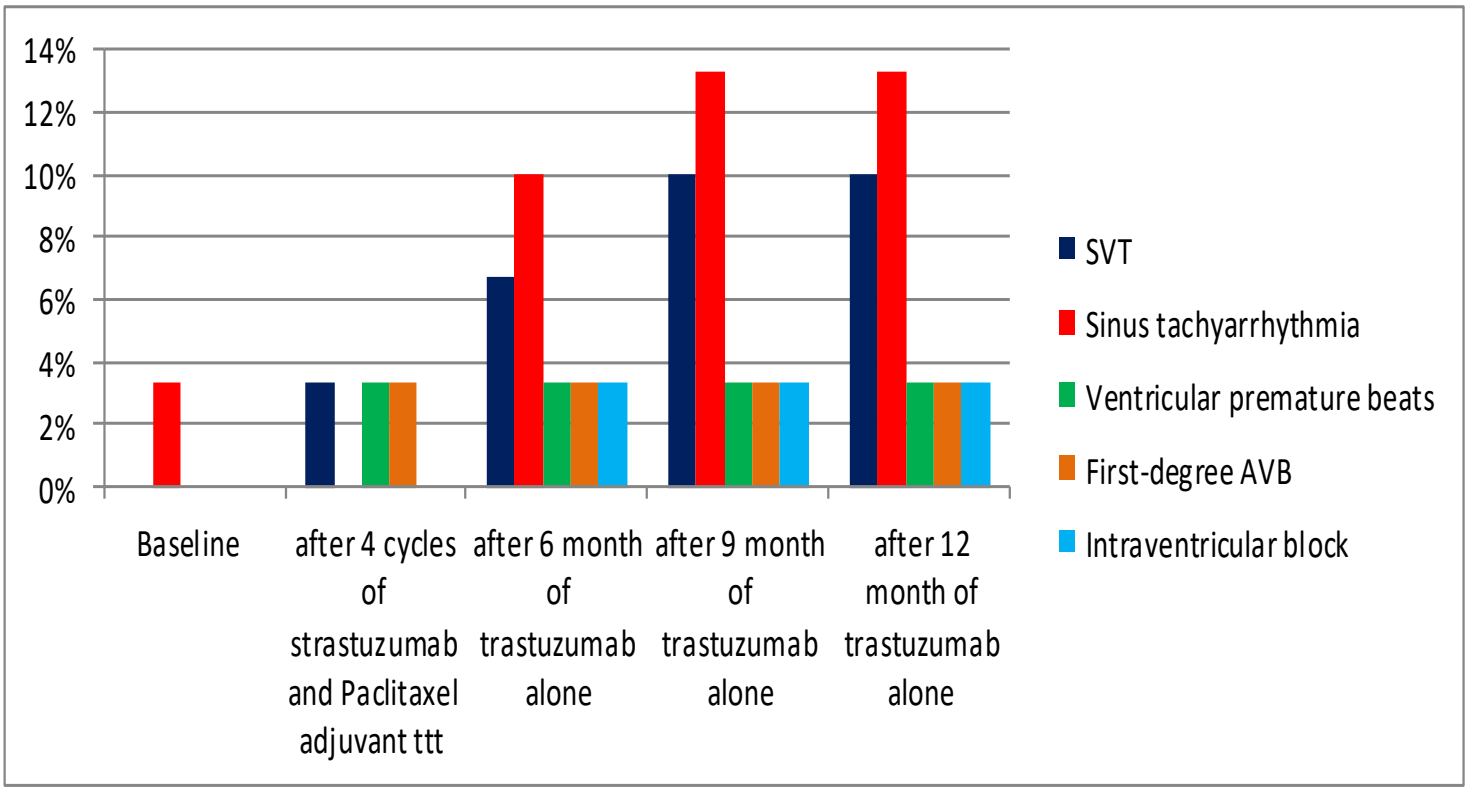

Fig.3. Cardiac arrhythmia in participating subject.

There was statistically insignificant difference in echocardiographic parameters in those who received trastuzumab and Paclitaxel adjuvant treatment for HER-2 positive breast cancer that baseline. However, there is statistically significant decline in LVEF%, MAPSE, TAPSE, E/E and RV FAC and significant increase in LVESD, LVEDD, LVISD, LA, E/A after treatment by trastuzumab alone for HER-2 positive breast cancer than baseline data before trastuzumab treatment,(**Table .3).**

Among our included subjects, 30% showed <5% reduction in EF% after 4 cycles of trastuzumab and Paclitaxel adjuvant treatment while 60% had <5% EF% reduction, 16.7% had 5-10% EF% reduction, 20% had 10-15% EF% reduction, and 3.3% had >15% EF% reduction after 12 month of trastuzumab alone, this difference was statistically significant. LVEF% ranged between 1.45-15.38% with mean value of 5.34±5.07 after 12 month of trastuzumab alone that was significantly higher than those who received trastuzumab and Paclitaxel adjuvant treatment, (**Table .4).**

Table 3. Echocardiographic data of participating subjects

Variables	Baseline		After 4 cycles trastuzumab and Paclitaxel adjuvant ttt		After 6 months trastuzumab alone		After 9 months trastuzumab alone		After 12 months trastuzumab alone		Baseline vs after adjuvant trastuzumab& Paclitaxel	Baseline vs after 12 m trastuzumab alone
	N=30		N=30		N=30		N=30		N=30		P-value	p-value
LVEF	61.37	3.66	60.8	3.48	59.8	3.73	58.8	4.16	57.97	4.59	0.579	0.001*
LVEDD	4.15	0.25	4.17	0.25	4.18	0.25	4.2	0.23	4.25	0.1	0.83	0.046*
LVESD	2.11	0.16	2.12	0.15	2.14	0.16	2.15	0.15	2.19	0.11	0.739	0.028*
IVSd	0.8	0.12	0.8	0.12	0.81	0.09	0.82	0.09	0.85	0.06	0.96	0.046*
LVPWd	0.8	0.1	0.8	0.1	0.81	0.08	0.82	0.07	0.84	0.04	0.963	0.047*
MAPSE	16.43	1.43	16.23	1.33	16.03	1.5	15.5	1.33	13.47	1.17	0.569	0.001*
LA	3.35	0.46	3.37	0.45	3.4	0.43	3.42	0.43	3.54	0.22	0.907	0.046*
E/A	1.46	0.29	1.47	0.29	1.48	0.29	1.49	0.29	1.58	0.12	0.993	0.041*
E/E	8.07	2.11	8.06	2.11	8.02	2.05	7.96	1.91	7.22	0.92	0.974	0.048*
TAPSE	25.4	2.51	25.2	2.75	24.23	2.58	23.43	1.63	21.7	1.73	0.735	0.001*
RVFAC	47.23	7.98	46.8	8.04	45.57	7.13	43.53	4.85	42.13	4.22	0.801	0.003*

LVEF: Left Ventricular Ejection Fraction, LVEDD: Left Ventricular End-Diastolic Dimension, LVESD: Left Ventricular End-Systolic Dimension, IVSd: Interventricular Septum thickness at end-diastole, LVPWd: Left Ventricular Posterior Wall thickness at end-diastole, MAPSE: Mitral Annular Plane Systolic Excursion, LA: Left Atrium, E/A: Ratio of early (E) to late (A) ventricular filling velocities, E/E: Ratio of early (E) mitral inflow velocity to early (E) mitral annular velocity, TAPSE: Tricuspid Annular Plane Systolic Excursion, RVFAC: Right Ventricular Fractional Area Change, * significant.

Table 4. EF% reduction rate after 4 cycles of trastuzumab and Paclitaxel adjuvant treatment and after 12 months of trastuzumab alone:

Variables		after 4 cycles of trastuzumab and Paclitaxel adjuvant ttt N=30		after 12 months of trastuzumab alone N=30		Test of sig
		N	%	N	%	P-value
LVEF% reduction	<5%	9	30%	18	60%	0.0001
	5-10%	0	0%	5	16.70%	
	10-15%	0	0%	6	20%	
	>15%	0	0%	1	3.30%	
LVEF% reduction	Range (median)	0-3 (0)		1.45-15.38 (1.8)		0.0001
	Mean ± SD	0.55±0.97		5.34±5.07		

LVEF%: Percentage of Left Ventricular Ejection Fraction, * significant.

Discussion

Our study comprised individuals aged 43-61 (mean 54.4±4.89) with tumor sizes ranging from 2.8-5.9 cm (mean 4.16±0.84). Invasive ductal carcinoma (80%), invasive lobular carcinoma (20%), and right-sided tumors (53.3%) predominated. Estrogen receptors were discovered in 66.7%, progesterone receptors in 60%, and Ki67 levels ranged from 7-34 (mean 14.6±9.01).

Hussain et al. (2019) studied trastuzumab cardiac safety in HER2-positive breast cancer patients, supporting our results. The median age was 54, ranging from 47-60. Mostly invasive ductal carcinoma (95%), invasive lobular carcinoma (5%). Patients have 47% progesterone receptors and 58% estrogen receptors.

Debien et al. (2023) examined the efficacy and safety of adjuvant paclitaxel and trastuzumab in Belgian and Italian node-negative HER2-positive BC patients with tumors between 0.5 and 2 cm. The median age was 59.5. Aged tumors were 0.5-2 cm 4. Invasive ductal carcinoma (86.3%) and lobular carcinoma (7.8%) predominated. Patients have 68.7% progesterone receptors and 85% estrogen receptors.

In our investigation, baseline ECG was unchanged. After 4 cycles of trastuzumab with Paclitaxel, rates rose to 16.7% and 53.3% after 12 months with trastuzumab alone. Trastuzumab alone caused greater ECG abnormalities than Paclitaxel adjuvant therapy (46.7% vs. 16.7%).

Piotrowski et al. (2013) studied cardiac changes in adjuvant trastuzumab-treated HER2-positive breast cancer patients. ECG issues increased considerably after bassline and trastuzumab alone.

We support **Yu et al. (2016)** who found a statistically significant increase in ECG abnormalities after bassline and trastuzumab/paclitaxel adjuvant treatment.

Our study found ECG changes in P-wave, ST-segment, T-wave, and QRS. The difference in T-wave alterations after 12 months of trastuzumab alone was statistically significant (20% vs 0%), however after 4 cycles of trastuzumab with Paclitaxel adjuvant therapy was not (16.7% vs 3.3%).

Our findings match **Dang et al. (2015)** who evaluated the effectiveness and safety of weekly pertuzumab and trastuzumab with paclitaxel. ECG after trastuzumab with pertuzumab and Paclitaxel adjuvant therapy was significantly different from baseline.

Our findings also support **Tolaney et al. (2021),** who investigated whether trastuzumab emtansine (T-DM1) was less hazardous than paclitaxel with TH. After trastuzumab alone and paclitaxel plus TH, ECGs differed statistically from baseline.

Our research found that baseline sinus tachycardia was 3.3% and rose to 16.7% following 4 cycles of trastuzumab plus Paclitaxel (containing SVT 3.3%, first-degree AVB 3.3%, and ventricular premature beats 3.3%). After 6 months of trastuzumab alone, it rose to 26.7% (SVT 6.7%, sinus tachycardia 10%, Ventricular premature beats 3.3%, First-degree AVB 3.3%), peaking at 33.3% after 9-12 months. Compared to baseline, arrhythmia increased 33% after 12 months of trastuzumab alone, although the difference following 4 cycles of trastuzumab + Paclitaxel was modest (16.7% vs 3.3%).

Consistent with **Dang et al. (2016),** our study found no statistically significant difference in arrhythmia after 4 cycles of trastuzumab and Paclitaxel compared to baseline.

In our study we found that there was no statistically significant difference in echocardiographic parameters in those who received trastuzumab and Paclitaxel adjuvant treatment for HER-2 positive breast cancer and baseline. However, there was statistically significant decline in LVEF%, MAPSE, TAPSE, E/E and RV FAC and significant increase in LVESD, LVEDD, LVISD, LA, E/A after treatment by trastuzumab alone for HER-2 positive breast cancer than baseline data before trastuzumab treatment.

Our results are consistent with, **Barroso-Sousa et al. (2022),** who aimed to determine cardiac outcomes of subjects on adjuvant trastuzumab emtansine vs paclitaxel in combination with trastuzumab for stage I HER2-positive breast cancer (ATEMPT). They reported that no significant association between these baseline characteristics and the incidence of significant asymptomatic LVEF decline or symptomatic LVSD was identified.

Dang et al. (2016), found that baseline LVEF values were between 50% and 55% in 40 (10%) patients, and greater than 55% in 366 (90%) patients. Overall, the majority of patients had a decline in LVEF from baseline of less than 10% (84% at 12 weeks; 80%, 6 months; and 74%, 1 year), and only a minority of patients had a decline in LVEF from baseline of 10% to 15% (7% at 12 weeks; 9%, 6 months; and 9%, 1 year) and greater than or equal to 16% (<1% at 12 weeks; 1%, 6 months; and 2%, 1 year).

Also, **Piotrowski et al. (2012),** who reported that echocardiography performed after 3 months, after 6 months, and after 9 months, Cardiac complications developed in 52 pts (20.55%) and included: asymptomatic left ventricle dysfunction (43), symptomatic heart failure (6), new asymptomatic LBBB (1); new negative T-waves in ECG (2). There was a progressive decline in left ventricular ejection fraction (LVEF) during treatment. So that there was statistically significant decline in LVEF ($p < 0.05$)

In our study we found that 30% showed <5% reduction in EF% after 4 cycles of trastuzumab and Paclitaxel adjuvant treatment while 60% had <5% EF% reduction, 16.7% had 5-10% EF% reduction, 20% had 10-15% EF% reduction, and 3.3% had >15% EF% reduction after 12 month of trastuzumab alone, this difference was statistically significant. LVEF% ranged between 1.45-15.38% with mean value of 5.34±5.07 after 12 month of trastuzumab

alone that was statistically significantly higher than those who received trastuzumab and Paclitaxel adjuvant treatment.

Our results are consistent with, **Schneider et al. (2015)**, who aimed to evaluate the safety of paclitaxel-trastuzumab adjuvant therapy for early-stage breast cancer, particularly with respect to CHF and LVEF. They found that LVEF reduction in trastuzumab alone was statistically significantly higher than those who received trastuzumab and Paclitaxel adjuvant treatment.

Also, **Huang et al. (2015),** who aimed to compare the efficacy and safety between epirubicin (E) and carboplatin (C) in combination with paclitaxel (P) and trastuzumab (H) in neoadjuvant setting. LVEF at baseline, and during neoadjuvant treatment after 2 and 4 cycles. They found that all patients in both groups maintained normal LVEF throughout the study. After 2 cycles, over 10% reduction of LVEF was observed in 5 patients (11.9%) in PCH group, while it was 3 patients (7.3%) in PCH group had over 10% LVEF reduction after 4 cycles.

As well, our results consistent with **Yu et al. (2016),** who found that LVEF was assessed by ECHO at baseline and every fourth cycle (every 3 months) and they found that no patients developed LVSD (grades 3 or 4). The mean LVEF at baseline was 64% (range: 50%–72%), and overall mean LVEF values remained stable throughout the study. The incidence of asymptomatic LVEF decline (both grade 2) was 3.0%. One patient developed an LVEF decline of 16% (a decrease from 72% at baseline to 55% at month 15), and 1 patient developed an LVEF of ,50% with a decline of 10%–15% from baseline (57% at baseline to 47% at month 9)

Furthermore, **Barroso-Sousa et al. (2022),** who reported that patients in the adjuvant trastuzumab emtansine arm experienced a significant asymptomatic left ventricular ejection fraction (LVEF) decline.

Conclusion

Our study evaluated cardiac toxicity of concurrent administration of Trastuzumab plus Paclitaxel in post operative treatment of HER-2 +ve Breast cancer. We revealed that regarding LVEF%, there was statistically significant higher after 12 months of trastuzumab alone than those who received trastuzumab and Paclitaxel adjuvant treatment. Also, we found that there was statistically significant higher number of patients who developed ECG abnormalities after trastuzumab alone than after trastuzumab and Paclitaxel adjuvant treatment

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