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Original Research Article

Evaluation of Troponin-T as a Biomarker for Early Detection of Anthracycline-Induced Cardiotoxicity in Breast Cancer Patients

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Abstract:

Background: Anthracycline-based chemotherapy is a cornerstone in breast cancer management but is correlated with the risk of cardiotoxicity, which may lead to asymptomatic myocardial injury or symptomatic heart failure. Early detection of subclinical cardiotoxicity is essential to prevent long-term cardiac complications. Cardiac Troponin-T (cTnT) is a sensitive biomarker for detecting myocardial injury and may serve as an early predictor of anthracycline-induced cardiotoxicity.

Aim: To assess cardiotoxicity in breast cancer patients receiving anthracycline-based chemotherapy using Troponin-T levels and echocardiographic parameters before and after treatment.

Methods: This prospective cross-sectional study was conducted at Dr. S. N. Medical College, Jodhpur (Rajasthan, India) over three years. A total of 250 female breast cancer patients scheduled for anthracycline therapy were enrolled. Baseline demographic, clinical, and cardiac parameters were recorded. Serum Troponin-T levels and echocardiography, including left ventricular ejection fraction (LVEF), were measured before initiation of chemotherapy and after completion of the regimen. Data were analyzed using SPSS version 23.0, with paired t-tests for continuous variables and Chi-square tests for categorical variables. A p-value <0.05 was considered significant.

Results: The mean age of participants was 49.8 ± 8.7 years. Post-chemotherapy, mean Troponin-T levels increased significantly from 0.012 ± 0.009 ng/mL to 0.046 ± 0.031 ng/mL ($p < 0.001$). Echocardiographic evaluation revealed a significant decline in LVEF from 64.1 ± 5.8% to 58.9 ± 6.3% ($p < 0.001$). A total of 52 patients (20.8%) developed cardiotoxicity, predominantly asymptomatic, with only 6 patients (2.4%) showing symptomatic heart failure. Post-treatment Troponin-T levels correlated negatively with LVEF ($r = –0.61$, $p < 0.001$), indicating higher Troponin-T was correlated with greater cardiac dysfunction.

Conclusion: Anthracycline-based chemotherapy is correlated with subclinical cardiotoxicity in a significant subset of breast cancer patients. Troponin-T serves as a sensitive early biomarker for myocardial injury and correlates with echocardiographic changes.

Recommendations: Routine monitoring of Troponin-T before, during, and after anthracycline therapy is recommended to facilitate early detection and timely management of cardiotoxicity, reducing the risk of long-term cardiac complications.

Keywords: Breast Cancer, Anthracycline, Cardiotoxicity, Troponin-T, Echocardiography.

Introduction

Breast cancer continues to be the most frequently diagnosed malignancy among women worldwide and remains a leading cause of cancer-related mortality [1]. Anthracyclines, including doxorubicin and epirubicin, form a cornerstone of chemotherapy for breast cancer due to their potent cytotoxic activity and proven survival benefits [2]. However, their therapeutic use is limited by a well-recognized risk of cardiotoxicity, which can present as asymptomatic ventricular dysfunction, arrhythmia, or overt heart failure [3]. The incidence of anthracycline-induced cardiotoxicity (ACT) varies between 10% and 26%, depending on the cumulative dose, patient comorbidities, and concurrent cardiotoxic treatments [4].

The mechanisms underlying ACT involve oxidative stress, mitochondrial injury, and myocyte apoptosis leading to irreversible myocardial damage [5]. Traditional monitoring through echocardiography and electrocardiography often detects cardiac dysfunction only after significant myocardial damage has occurred [6]. Hence, identifying reliable biomarkers that can detect cardiac injury at a

subclinical stage has become a major focus of recent research. Among these, cardiac troponins (T and I) are considered the most specific indicators of myocardial injury [7]. Even minimal elevations in serum troponin levels during chemotherapy have been shown to predict later declines in (LVEF) and development of symptomatic heart failure [8].

Recent prospective studies have demonstrated that serial monitoring of high-sensitivity Troponin-T (hs-cTnT) during anthracycline therapy can detect early myocardial injury before echocardiographic changes become evident [9]. Integration of biomarker surveillance with advanced imaging techniques, such as global longitudinal strain (GLS) by echocardiography, further enhances early detection and risk stratification [10]. Early identification of subclinical cardiac dysfunction allows timely initiation of cardioprotective interventions, modification of chemotherapy regimens, and prevention of long-term cardiac sequelae.

Despite the growing evidence, data on Troponin-T monitoring in the Indian population are limited, and routine cardiac biomarker surveillance is not yet a standard practice in most oncology centers. Considering the widespread use of anthracyclines in breast cancer and the potential for preventable cardiac morbidity, further clinical evaluation is warranted. Therefore, the present study aims to assess Troponin-T as an early biomarker for detecting cardiotoxicity in breast cancer patients treated with anthracycline-based chemotherapy and to correlate biochemical changes with echocardiographic parameters before and after treatment over a defined follow-up period.

Methodology

Type of Study: The research was designed as a prospective cross-sectional study.

Study Setting: The study was conducted in the Departments of Oncology and Cardiology at Dr. S. N. Medical College, Jodhpur (Rajasthan), India. The institution serves as a tertiary care center catering to a large population of western Rajasthan, equipped with modern diagnostic and therapeutic facilities including echocardiography, ECG monitoring, and laboratory support for biochemical marker estimation such as Troponin-T.

Study Duration: The study was carried out over a period of three years, from January 2022 to December 2024, which included patient recruitment, baseline evaluation, chemotherapy administration, follow-up testing, and data analysis.

Participants: A total of 250 female patients diagnosed with breast cancer and scheduled to receive anthracycline-based chemotherapy were enrolled in the study. All participants were followed up at two time points — before initiation of chemotherapy and after completion of the planned anthracycline regimen — to evaluate changes in Troponin-T levels and cardiac function parameters.

Inclusion Criteria

1. Female patients aged 18 to 65 years with histopathologically confirmed breast cancer.
2. Patients planned for anthracycline-based chemotherapy (e.g., doxorubicin or epirubicin).
3. Patients with normal baseline cardiac function as determined by echocardiography and ECG.
4. Patients who provided written informed consent for participation and follow-up.

Exclusion Criteria

1. Patients with pre-existing cardiac diseases, such as ischemic heart disease, arrhythmia, or valvular disorders.
2. Patients receiving concurrent radiotherapy to the chest region.
3. Patients on other potentially cardiotoxic drugs or with renal/hepatic impairment.
4. Patients lost to follow-up or with incomplete clinical or biochemical data.

Bias and Confounding Control: To minimize bias, all biochemical measurements were performed in the same laboratory using standardized assays and quality controls. The same observer team assessed echocardiographic and ECG parameters to reduce inter-observer variability. Data collectors were blinded to treatment cycles during analysis. Potential confounders such as age, baseline ejection fraction, and cumulative anthracycline dose were adjusted during statistical analysis.

Data Collection: Baseline demographic, clinical, and treatment details were recorded using a structured proforma. Blood samples were collected for serum Troponin-T estimation prior to initiation of chemotherapy and within 7 days after completion of the final cycle. Cardiac evaluation, including ECG and echocardiography, was performed at both time points to correlate biochemical findings with functional cardiac changes. Data were compiled from hospital records, laboratory reports, and follow-up visits.

Procedure: After obtaining ethical clearance, eligible patients were enrolled prior to starting anthracycline therapy. Standard chemotherapy regimens were administered under oncologist supervision. Blood samples (3–5 mL) were collected in plain vials and analyzed for Troponin-T levels using an enzyme-linked immunosorbent assay (ELISA) method. Any rise in Troponin-T above the upper reference limit (>0.04 ng/mL) was considered indicative of subclinical myocardial injury. Echocardiography was performed to assess (LVEF), and cardiotoxicity was classified based on absolute

LVEF reduction ≥10% or below 50%. Patients were monitored for clinical symptoms of cardiac dysfunction throughout therapy.

Statistical Analysis: Data were entered and analyzed using (SPSS) version 23.0. Continuous variables such as Troponin-T levels and LVEF were expressed as mean ± standard deviation (SD). Pre- and post-treatment values were compared using paired t-test or Wilcoxon signed-rank test for non-parametric data. Categorical variables were analyzed using the Chi-square test or Fisher's exact test. A p-value <0.05 was considered statistically significant. Correlation between Troponin-T levels and echocardiographic changes was assessed using Pearson's correlation coefficient.

Results

A total of 250 breast cancer patients receiving anthracycline-based chemotherapy were enrolled and followed up before and after treatment. The mean age of participants was 49.8 ± 8.7 years (range 28–65 years). Most patients (60%) were between 41–55 years of age. Hypertension was present in 22%, diabetes mellitus in 18%, and both comorbidities in 6% of participants.

Table 1: Baseline Demographic and Clinical Characteristics (n = 250)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	18–40	60	24.0
	41–55	150	60.0
	>55	40	16.0
Mean Age ± SD		49.8 ± 8.7	
Comorbidities	None	135	54.0
	Hypertension	55	22.0
	Diabetes Mellitus	45	18.0
	Both HTN + DM	15	6.0
ECOG Performance Status (0–2)	0	115	46.0
	1	90	36.0
	2	45	18.0

The study population predominantly comprised middle-aged women with good performance status. Nearly half had no comorbid illness, ensuring minimal baseline cardiac risk factors.

Changes in Troponin-T Levels Before and After Anthracycline Therapy: Baseline serum Troponin-T levels were within the normal range in all participants prior to chemotherapy. After completion of anthracycline treatment, 66 patients (26.4%) showed elevated Troponin-T levels (>0.04 ng/mL). The mean Troponin-T increased significantly from 0.012 ± 0.009 ng/mL pre-treatment to 0.046 ± 0.031 ng/mL post-treatment ($p < 0.001$).

Table 2: Comparison of Serum Troponin-T Levels Before and After Treatment (n = 250)

Parameter	Pre-Treatment (Mean ± SD)	Post-Treatment (Mean ± SD)	Mean Difference	p-Value
Troponin-T (ng/mL)	0.012 ± 0.009	0.046 ± 0.031	+0.034	<0.001*

*Paired t-test applied; statistically significant ($p < 0.05$).

There was a nearly four-fold increase in mean Troponin-T levels following anthracycline therapy, indicating biochemical evidence of subclinical myocardial injury in a significant subset of patients.

Echocardiographic Changes Before and After Treatment: Left ventricular ejection fraction (LVEF) was measured before and after treatment to detect cardiac dysfunction. The mean LVEF decreased from 64.1 ± 5.8% at baseline to 58.9 ± 6.3% post-treatment ($p < 0.001$).

Cardiotoxicity, defined as ≥10% absolute reduction in LVEF or LVEF <50%, was detected in 52 patients (20.8%).

Table 3: Comparison of Echocardiographic Findings Before and After Treatment (n = 250)

Parameter	Pre-Treatment (Mean ± SD)	Post-Treatment (Mean ± SD)	Mean Change	p-Value
LVEF (%)	64.1 ± 5.8	58.9 ± 6.3	–5.2	<0.001*
Fractional Shortening (%)	33.8 ± 4.2	30.5 ± 4.5	–3.3	0.002*
LV End-Diastolic Diameter (mm)	47.3 ± 3.4	49.1 ± 3.8	+1.8	0.021*

*Paired t-test applied; statistically significant.

A significant decline in both LVEF and fractional shortening was noted, suggesting mild but measurable systolic dysfunction after anthracycline exposure.

Correlation Between Troponin-T and Echocardiographic Changes: A significant negative correlation was observed between post-treatment Troponin-T levels and LVEF ($r = –0.61$, $p < 0.001$), indicating that higher Troponin-T values were correlated with a greater decline in left ventricular function.

Table 4: Correlation Between Post-Treatment Troponin-T and LVEF (n = 250)

Variable Pair	Correlation Coefficient (r)	p-Value	Interpretation
Troponin-T vs. LVEF	–0.61	<0.001	Strong negative correlation

This strong inverse relationship reinforces Troponin-T as a reliable early biomarker for predicting anthracycline-induced cardiac dysfunction even before overt clinical symptoms appear.

Incidence and Severity of Cardiotoxicity: Among the 250 patients, 52 (20.8%) developed cardiotoxicity. Based on Common Terminology Criteria for Adverse Events (CTCAE v5.0):

- Grade 1 (Asymptomatic, only biomarker rise): 34 patients (13.6%)
- Grade 2 (Mild LVEF drop, no symptoms): 12 patients (4.8%)
- Grade 3 (Symptomatic heart failure): 6 patients (2.4%)

No patient developed grade 4 or fatal events during follow-up.

Table 5: Distribution of Cardiotoxicity Severity Among Participants (n = 250)

Grade of Cardiotoxicity	Criteria	Frequency (n)	Percentage (%)
Grade 0	No toxicity	198	79.2
Grade 1	Elevated Troponin-T only	34	13.6
Grade 2	LVEF ↓ <10% without symptoms	12	4.8
Grade 3	Symptomatic heart failure	6	2.4

The majority of cardiotoxic events were mild and asymptomatic, detected only through biochemical or echocardiographic monitoring, highlighting the importance of early marker-based surveillance.

Summary of Key Findings

- Mean Troponin-T levels increased significantly after anthracycline chemotherapy ($p < 0.001$).
- 20.8% of patients exhibited measurable cardiotoxicity based on LVEF reduction.
- Troponin-T elevation preceded echocardiographic changes, suggesting early myocardial injury detection.
- A strong negative correlation ($r = –0.61$) between Troponin-T and LVEF validates Troponin-T as a sensitive predictive biomarker.

Discussion

Out of 250 breast cancer patients enrolled in this study, the mean age was 49.8 years, with the majority belonging to the 41–55 years age group. Most participants had good baseline performance status and were free from significant comorbidities, minimizing potential confounding factors for cardiac dysfunction. Baseline cardiac evaluation revealed normal left ventricular function and normal serum Troponin-T levels in all patients, establishing a reliable pre-therapy reference point.

Following anthracycline-based chemotherapy, there was a significant increase in serum Troponin-T levels, from a mean of 0.012 ng/mL before treatment to 0.046 ng/mL after completion ($p < 0.001$). Approximately 26.4% of patients exhibited elevated Troponin-T levels beyond the normal limit, indicating early biochemical evidence of myocardial injury. These elevations occurred even in some patients without any clinical symptoms, highlighting the sensitivity of Troponin-T as an early biomarker of anthracycline-induced cardiotoxicity.

Echocardiographic assessments showed a notable decline in mean left ventricular ejection fraction (LVEF) from 64.1% to 58.9% post-treatment ($p < 0.001$). Cardiotoxicity, defined by a ≥10% drop in LVEF or an absolute value below 50%, was observed in 20.8% of participants. Fractional shortening also declined significantly, supporting the presence of subclinical systolic dysfunction. However, only a small proportion (2.4%) of patients developed clinically symptomatic cardiac failure, suggesting that early detection through biomarkers and imaging can prevent severe cardiac complications.

A statistically significant negative correlation ($r = –0.61$, $p < 0.001$) was found between post-treatment Troponin-T levels and LVEF, indicating that higher Troponin-T concentrations were correlated with a greater reduction in cardiac function. This association confirms that Troponin-T elevation serves as an early predictor of impending

cardiotoxicity, often preceding measurable echocardiographic changes.

Overall, the study findings demonstrate that a substantial subset of breast cancer patients receiving anthracycline therapy develop subclinical cardiotoxicity detectable by Troponin-T monitoring. The correlation between biochemical and functional cardiac parameters emphasizes the importance of routine cardiac surveillance. Incorporating Troponin-T estimation into follow-up protocols could facilitate early intervention, modification of therapy, and prevention of irreversible cardiac damage. These results reaffirm Troponin-T as a valuable, sensitive, and non-invasive biomarker for early cardiotoxicity detection in patients undergoing anthracycline-based chemotherapy.

Recent investigations have highlighted the clinical utility of (hs-TnT) for the early detection of anthracycline-induced cardiotoxicity in breast cancer patients. A prospective study demonstrated that serum hs-TnT levels rise significantly after the first cycles of anthracycline chemotherapy, preceding any measurable reduction in (LVEF). This supports hs-TnT as an early subclinical biomarker for myocardial injury that may predict future cardiac dysfunction [11].

Similarly, Garam et al. reported that elevations in hs-TnT levels occurred prior to echocardiographic evidence of cardiotoxicity, reinforcing its role in detecting cardiac injury at a stage when interventions could be most effective [12]. The study also emphasized that baseline troponin concentrations were predictive of later cardiac complications, suggesting potential value for risk stratification.

Further, Oikonomou et al. found that combining hs-TnT with global longitudinal strain (GLS) analysis using echocardiography improved sensitivity for detecting early myocardial impairment. The combined approach enhanced diagnostic accuracy over either modality alone, enabling clinicians to identify patients at higher risk of cardiac damage earlier in therapy [13].

In another study, serial measurement of hs-TnT throughout chemotherapy cycles was used to guide early cardioprotective treatment. Kim et al. showed that integrating troponin monitoring into routine oncologic care allowed for timely initiation of agents such as ACE inhibitors or beta-blockers, resulting in reduced progression of cardiac dysfunction and fewer declines in LVEF [14].

Finally, Koutsoukis et al. proposed a multimodal risk assessment strategy, combining hs-TnT with N-terminal pro-B-type natriuretic peptide (NT-proBNP) and advanced cardiac imaging. This comprehensive model improved the predictive performance for early cardiotoxicity and allowed for individualized monitoring in breast cancer patients receiving anthracyclines [15]. Collectively, these findings underscore that high-sensitivity Troponin-T is a reliable and sensitive biomarker for detecting early myocardial injury due to anthracyclines. When combined with strain imaging and natriuretic peptides, hs-TnT offers an effective strategy for early diagnosis, prevention, and management of chemotherapy-induced cardiotoxicity in breast cancer patients.

Conclusion

This study demonstrates that anthracycline-based chemotherapy in breast cancer patients is correlated with a significant rise in Troponin-T levels and a measurable decline in left ventricular function. Elevated Troponin-T serves as an early and sensitive indicator of subclinical cardiotoxicity, often preceding echocardiographic changes. Routine monitoring of Troponin-T during chemotherapy can enable timely detection and management of cardiac injury, thereby reduce the risk of irreversible heart damage and improve patient outcomes.

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