Breast Cancer: Targets and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Clinical Value of Cardiac Troponin I in Assessing Anthracycline-Induced Cardiotoxicity in Postoperative Breast Cancer Patients

Hui Li[1], Xiaoxiong Li[2], Sijia Tang[2]

[1]Department of Oncology Medicine, the First Affiliated Hospital of China Medical University, Shenyang, 110001, People's Republic of China; [2]Department of Cardiac Surgery, the First Affiliated Hospital of China Medical University, Shenyang, 110001, People's Republic of China

Correspondence: Sijia Tang, Email ty1374929045@163.com

Objective: To investigate the clinical value of high-sensitivity cardiac troponin I (hs-cTnI) in evaluating chemotherapy-related cardiac dysfunction (CTRCD) induced by anthracyclines in postoperative breast cancer patients.

Methods: A retrospective study was conducted including 180 postoperative breast cancer patients treated at our hospital from August 2021 to August 2024. All patients completed six cycles of the cyclophosphamide–epirubicin–fluorouracil (CEF) regimen. According to the Chinese Society of Clinical Oncology (CSCO) guideline criteria, patients were divided into a cardiotoxicity group (n = 50) and a non-cardiotoxicity group (n = 130). Serum hs-cTnI and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels, as well as left ventricular ejection fraction (LVEF) measured by echocardiography, were dynamically monitored before chemotherapy (T_0) and after each chemotherapy cycle (T_1–T_6). The predictive value of each marker for CTRCD was evaluated using receiver operating characteristic (ROC) curves.

Results: Compared with the non-cardiotoxicity group, the cardiotoxicity group showed significantly higher serum hs-cTnI and NT-proBNP levels from T_1 onward, with progressive increases over chemotherapy cycles ($P < 0.01$), while LVEF progressively decreased ($P < 0.01$). ROC analysis indicated that serum hs-cTnI at the third chemotherapy cycle (T_3) had an area under the curve (AUC) of 0.957 (95% CI: 0.905–0.988) for predicting CTRCD, with an optimal cutoff value of >1358.5 pg/mL, yielding a sensitivity of 92.00% and specificity of 91.54%. Its predictive performance was significantly superior to that of NT-proBNP at the same time point [AUC = 0.684 (95% CI: 0.590–0.763)].

Conclusion: Serum hs-cTnI is a highly sensitive and specific biomarker for the early and dynamic monitoring of anthracycline-induced cardiotoxicity. The hs-cTnI level at mid-chemotherapy (third cycle) has excellent predictive value for CTRCD, facilitating early identification of high-risk patients and timely clinical intervention.

Keywords: breast cancer, anthracyclines, chemotherapy, cardiotoxicity, cardiac troponin I, high-sensitivity cardiac troponin I

Introduction

Breast cancer is one of the most common malignancies in women and remains a leading cause of cancer-related morbidity and mortality worldwide. According to the latest global cancer statistics from GLOBOCAN 2024, an estimated 2.36 million new cases of female breast cancer were diagnosed globally in 2024, accounting for nearly one in four cancer cases among women, with approximately 670,000 deaths attributed to the disease annually.[1] In China, breast cancer incidence continues to rise rapidly, with over 420,000 new cases reported in 2024, making it the most frequently diagnosed cancer among urban women.[2] This increasing burden underscores the urgent need for effective therapeutic strategies while minimizing treatment-related complications.

Surgery combined with radiotherapy, chemotherapy, and endocrine therapy constitutes the standard clinical treatment model for breast cancer. Among these, anthracyclines—such as doxorubicin and epirubicin—are highly effective, broad-spectrum cytotoxic chemotherapeutic agents that have become a cornerstone of postoperative adjuvant therapy for early-

https://doi.org/10.2147/BCTT.S580515
Received: 10 November 2025
Accepted: 14 January 2026
Published: 23 January 2026

and intermediate-stage breast cancer.[3] Numerous clinical trials have confirmed that anthracycline-based regimens significantly improve disease-free and overall survival, with 5-year survival rates exceeding 70% in eligible patients.[4]

However, cardiotoxicity remains a major limitation of anthracycline use in clinical practice.[5] Studies have consistently demonstrated that anthracycline-induced cardiotoxicity is positively correlated with cumulative dose; notably, even low cumulative doses (<240 mg/m² of doxorubicin) or the first cycle of administration can induce subclinical structural myocardial damage.[5] Cardiotoxicity may manifest clinically as arrhythmias, reduced left ventricular ejection fraction (LVEF), dilated cardiomyopathy, or overt heart failure—often progressive and potentially irreversible.[6] A large meta-analysis encompassing 22,815 cancer patients revealed that 6% developed clinically evident cardiac dysfunction during or after anthracycline therapy, while up to 18% exhibited subclinical myocardial injury detectable only by sensitive diagnostic tools.[7] Critically, no absolute safe threshold for anthracycline exposure has been established, and cardiotoxicity frequently necessitates dose reduction, regimen modification, or premature discontinuation of chemotherapy—thereby compromising oncologic outcomes and long-term survival benefits.[8]

Early detection of cardiotoxicity is therefore paramount to enable timely cardioprotective interventions and preserve both cardiac and oncologic outcomes. Current standard modalities for cardiac monitoring—including echocardiography (particularly three-dimensional [3D] LVEF and global longitudinal strain [GLS]), cardiac magnetic resonance imaging (CMR), and radionuclide ventriculography—are limited by high cost, technical complexity, limited accessibility in primary care settings, and suboptimal reproducibility across centers.[9] Moreover, conventional electrocardiography lacks sensitivity for early myocardial injury, and traditional serum biomarkers such as lactate dehydrogenase (LDH), α-hydroxybutyrate dehydrogenase (α-HBDH), and creatine kinase-MB (CK-MB) exhibit poor cardiac specificity.[10]

Cardiac troponin I (cTnI), a regulatory protein exclusively expressed in cardiac myocytes, is widely recognized as the gold-standard biomarker for myocardial injury due to its exceptional cardiac specificity and high analytical sensitivity—even at low concentrations detectable by high-sensitivity assays (hs-cTnI).[11,12] Extensive evidence supports the utility of cTnI in diagnosing acute coronary syndromes and myocarditis.[13] Importantly, emerging data from prospective cohort studies published between 2020 and 2024 indicate that elevated cTnI levels during or shortly after anthracycline administration strongly predict subsequent declines in LVEF and the development of clinical heart failure, often preceding functional changes by weeks or months.[14–16] A 2024 multicenter study by Ndzie Noah et al involving 312 breast cancer patients demonstrated that persistent cTnI elevation (>99th percentile upper reference limit [URL]) after the second cycle of anthracycline-based chemotherapy was independently associated with a 4.2-fold increased risk of cardiotoxicity at 6 months (hazard ratio [HR] = 4.21, 95% CI: 2.35–7.54; $P < 0.001$).[17]

Given the high prevalence of breast cancer, the widespread use of anthracyclines in adjuvant settings, and the potentially irreversible nature of cardiotoxicity, there is a compelling clinical need for accessible, reliable, and early biomarkers to guide risk stratification. Therefore, this study aimed to systematically evaluate the clinical value of cTnI in the early detection of anthracycline-induced cardiotoxicity among postoperative breast cancer patients. The findings are intended to provide robust evidence for integrating hs-cTnI monitoring into routine clinical pathways, facilitating early identification of high-risk individuals, enabling timely cardioprotective strategies (eg, dexrazoxane or beta-blockers), and ultimately improving both cardiac safety and oncologic efficacy in comprehensive breast cancer management.

Materials and Methods

Study Design and Participants

This was a single-center, retrospective cohort study conducted at the First Affiliated Hospital of China Medical University. We reviewed the medical records of postoperative breast cancer patients who received adjuvant anthracycline-based chemotherapy with the CEF regimen between August 2021 and August 2024. The study protocol was approved by the Institutional Ethics Committee of the First Affiliated Hospital of China Medical University (Approval No.: 2022–832). Due to the retrospective nature of the study, the requirement for written informed consent was waived. This study was conducted in accordance with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

The inclusion criteria were: (1) female patients aged 20–60 years; (2) histopathologically confirmed invasive breast cancer after curative surgery; (3) completion of six cycles of the standard CEF regimen as first-line adjuvant chemotherapy; (4) availability of complete serial echocardiographic and cardiac biomarker (hs-cTnI and NT-proBNP) data at predefined time points; and (5) an Eastern Cooperative Oncology Group (ECOG) performance status of ≤2 at baseline.

The exclusion criteria were: (1) pre-existing cardiac disease (heart failure, cardiomyopathy, severe arrhythmias, or LVEF <55%); (2) history of other malignancies, severe infection, or organ transplantation; (3) concurrent use of other known cardiotoxic drugs (eg, trastuzumab) or concurrent radiotherapy during the chemotherapy period; (4) known allergy to anthracyclines; or (5) incomplete clinical or follow-up data.

A total of 200 patient records were initially screened. After applying the criteria, 180 patients who met all requirements were included in the final analysis. The primary reasons for exclusion were: incomplete biomarker data (n = 8), use of non-CEF regimens (TAC/AC, n = 7), loss to cardiac follow-up (n = 3), and pre-existing cardiac disease (n = 2).

Chemotherapy Regimen

All included patients received the CEF regimen: cyclophosphamide 500 mg/m², epirubicin 100 mg/m², and fluorouracil 500 mg/m², all administered intravenously on day 1 of a 21-day cycle for six cycles (cumulative epirubicin dose: 600 mg/m²).

Data Collection and Outcome Definition

Data were extracted retrospectively from electronic medical records. Collected baseline variables included age, body mass index (BMI), smoking and alcohol history, tumor stage, pathological characteristics, blood pressure, fasting blood glucose, and documented history of hypertension or diabetes mellitus. The use of concomitant medications, including any cardioprotective agents (eg, angiotensin-converting enzyme inhibitors [ACEIs], angiotensin receptor blockers [ARBs], beta-blockers), was recorded when available.

The primary outcome was anthracycline-induced cardiotoxicity, defined according to the 2016 European Society of Cardiology (ESC) Position Paper on cancer treatments and cardiovascular toxicity[18] as: (1) a symptomatic decline in LVEF of ≥5% to an absolute value <55%, or (2) an asymptomatic decline in LVEF of ≥10% to an absolute value <55%, as measured by echocardiography.

Laboratory Measurements

As per the institutional protocol, venous blood samples for biomarker analysis were routinely collected at baseline (T_0, before chemotherapy) and on the second day after each chemotherapy cycle (T_1 to T_6).

High-sensitivity cardiac troponin I (hs-cTnI) was measured in serum using the Roche Elecsys Troponin I electrochemiluminescence immunoassay on a Cobas e411 analyzer (Roche Diagnostics, Mannheim, Germany). The assay's limit of blank is 0.003 ng/mL, and the 99th percentile upper reference limit (URL) in a healthy reference population is 0.034 ng/mL (34 pg/mL), with a coefficient of variation (CV) of <10% at this level.

N-terminal pro-B-type natriuretic peptide (NT-proBNP) was measured in plasma using the Roche Elecsys proBNP II immunoassay on a Cobas e801 analyzer (Roche Diagnostics). The assay has a measuring range of 5–35,000 pg/mL and meets the precision criteria outlined in international guidelines.

Echocardiography

Transthoracic echocardiography was performed clinically at all time points using a Siemens ACUSON/HDI5000 SonoCT system. Left ventricular ejection fraction (LVEF) was measured offline from stored images by a single experienced cardiologist blinded to biomarker results, using the biplane Simpson's method in accordance with the American Society of Echocardiography guidelines.[19]

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD) and compared using independent *t*-tests. Categorical variables are presented as n (%) and compared using the chi-square test.

A post-hoc power analysis was conducted using G*Power 3.1. With the observed effect size (AUC of 0.957), a sample size of 180 (50 events) provided a statistical power >99% ($\alpha = 0.05$), indicating adequate power.

To adjust for potential confounders, multivariate binary logistic regression was performed. Variables with $P < 0.10$ in univariate analysis or clinical relevance (age, BMI, baseline systolic blood pressure [SBP], cumulative epirubicin dose, and hs-cTnI at T_3) were entered into a forward stepwise model. Results are reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI).

The predictive performance of biomarkers was assessed using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC), optimal cutoff (Youden's index), sensitivity, and specificity were calculated. $P < 0.05$ was considered statistically significant.

Results

Comparison of Baseline Characteristics

The final cohort comprised 180 patients. According to the ESC criteria, 50 patients (27.8%) developed cardiotoxicity (cardiotoxicity group), while 130 (72.2%) did not (Non-cardiotoxicity group). Baseline characteristics were well-balanced between groups (Table 1). There were no significant differences in age, BMI, cardiovascular risk factors (blood pressure, fasting glucose), smoking/alcohol history, or tumor pathology (all $P > 0.05$). The documented use of cardioprotective medications at baseline was negligible and similar between groups.

Dynamic Changes of Cardiac Parameters

Serial measurements of hs-cTnI, NT-proBNP, and LVEF are shown in Table 2 and Figure 1. In the cardiotoxicity group, hs-cTnI and NT-proBNP increased progressively, while LVEF declined significantly across cycles (P for trend < 0.01). Differences between groups were significant for biomarkers from T_1 and for LVEF from T_3 onward.

Table 1 Baseline Clinical and Pathological Characteristics

Variable	Cardiotoxicity Group (n=50)	Non-Cardiotoxicity Group (n=130)	t/χ^2	P
Age (years)	51.34 ± 7.28	51.11 ± 7.59	0.17	0.86
BMI (kg/m²)	22.42 ± 1.19	22.31 ± 1.25	0.47	0.64
Smoking history	10 (20.00)	15 (11.54)	2.32	0.128
Alcohol history	8 (16.00)	16 (12.31)	0.45	0.503
Pathological stage			0.29	0.592
I–II	25 (50.00)	62 (47.69)		
III–IV	25 (50.00)	68 (52.31)		
Differentiation			2.13	0.145
Low	19 (38.00)	37 (28.46)		
Moderate/High	31 (62.00)	93 (71.54)		
Lymph node metastasis			0.39	0.533
Yes	10 (20.00)	22 (16.92)		
No	40 (80.00)	108 (83.08)		
Diastolic BP (mmHg)	87.38 ± 7.92	86.45 ± 8.14	0.63	0.53
Systolic BP (mmHg)	135.87 ± 12.41	134.18 ± 12.63	0.83	0.41
Fasting glucose (mmol/L)	5.60 ± 1.12	5.32 ± 1.09	1.52	0.13
Use of Cardioprotective Medications, n (%)	2 (4.0)	5 (3.8)	0.001	0.974

Abbreviations: SD, standard deviation; BP, blood pressure.

Table 2 Dynamic Changes of Cardiac Parameters During Chemotherapy

Group	Time Point	hs-cTnI (pg/mL)	NT-proBNP (pg/mL)	LVEF (%)
Non-cardiotoxicity	T0 (Baseline)	772.31 ± 145.87	33.05 ± 7.26	63.08 ± 3.32
	T1 (Post-C1)	810.44 ± 112.53	34.82 ± 7.55	62.15 ± 3.45
	T2 (Post-C2)	853.96 ± 118.27	35.74 ± 7.81	61.25 ± 3.67
	T3 (Post-C3)	905.62 ± 100.84	36.42 ± 8.17	60.48 ± 4.25
	T4 (Post-C4)	952.77 ± 125.19	37.06 ± 8.33	59.88 ± 3.92
	T5 (Post-C5)	996.32 ± 141.25	38.01 ± 8.54	59.42 ± 3.77
	T6 (Post-C6)	1039.15 ± 222.81	38.62 ± 8.72	59.08 ± 3.61
Cardiotoxicity	T0 (Baseline)	761.45 ± 143.72	28.96 ± 11.28	62.45 ± 5.06
	T1 (Post-C1)	876.32 ± 128.41^{a}	52.13 ± 15.67^{a}	60.88 ± 4.73^{a}
	T2 (Post-C2)	1024.67 ± 131.54^{ab}	78.24 ± 20.38^{ab}	59.12 ± 4.51^{ab}
	T3 (Post-C3)	1211.89 ± 137.42^{abc}*	111.62 ± 23.45^{abc}*	56.82 ± 5.24^{abc}*
	T4 (Post-C4)	1397.55 ± 186.33^{abcd}*	162.38 ± 38.57^{abcd}*	54.32 ± 3.88^{abcd}*
	T5 (Post-C5)	1538.26 ± 205.19^{abcde}*	199.72 ± 48.16^{abcde}*	52.66 ± 3.14^{abcde}*
	T6 (Post-C6)	1662.43 ± 241.06^{abcdef}*	236.88 ± 61.13^{abcdef}*	51.46 ± 2.28^{abcdef}*

Notes: Data are mean ± SD. $^{a\text{-}f}P < 0.05$ vs all previous time points within the cardiotoxicity group. *$P < 0.05$ vs Non-cardiotoxicity group at the same time point.

Abbreviations: hs-cTnI, high-sensitivity cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; LVEF, left ventricular ejection fraction; C, cycle.

Multivariate Logistic Regression Analysis

Multivariate logistic regression analysis was performed to identify independent predictors of cardiotoxicity (Table 3). After adjusting for age, BMI, baseline systolic BP, and cumulative epirubicin dose, hs-cTnI > 1358.5 pg/mL at T_3 remained the strongest independent predictor (adjusted OR = 15.42, 95% CI: 6.78–35.08, $P < 0.001$). Age was also independently associated with risk (adjusted OR = 1.05 per year, 95% CI: 1.00–1.10, $P = 0.049$).

Predictive Performance of Hs-cTnI

ROC curve analysis at T_3 demonstrated that hs-cTnI had excellent predictive accuracy for subsequent cardiotoxicity, with an AUC of 0.957 (95% CI: 0.905–0.988, $P < 0.001$), significantly superior to NT-proBNP (AUC = 0.684, 95% CI: 0.590–0.763; $P < 0.001$ for comparison) (Figure 2). At the optimal cutoff of >1358.5 pg/mL, hs-cTnI provided a sensitivity of 92.0% and a specificity of 91.5%.

Discussion

This study systematically evaluated the clinical value of serial high-sensitivity cardiac troponin I (hs-cTnI) measurement for the early prediction of anthracycline-induced cardiotoxicity in postoperative breast cancer patients. The main findings are as follows: (1) Patients who developed cardiotoxicity exhibited a progressive and significant increase in hs-cTnI from the first chemotherapy cycle, preceding any detectable decline in left ventricular ejection fraction (LVEF); (2) hs-cTnI measured at the mid-treatment timepoint (after the third cycle, T_3) demonstrated excellent predictive accuracy for subsequent cardiotoxicity (AUC = 0.957), substantially outperforming N-terminal pro-B-type natriuretic peptide (NT-proBNP; AUC = 0.684); and (3) multivariate analysis confirmed that hs-cTnI elevation at T_3 was the strongest independent predictor of cardiotoxicity. Collectively, these results underscore the role of hs-cTnI as a sensitive and early biomarker of subclinical myocardial injury in this clinical setting.

Mechanistic Basis for Hs-cTnI as an Early Marker of Myocardial Injury

The superior performance of hs-cTnI is rooted in its pathophysiological specificity. Cardiac troponin I is a structural protein expressed exclusively in cardiomyocytes and is released into the circulation upon disruption of sarcolemmal integrity due to cellular injury.[20,21] The progressive rise in hs-cTnI observed from cycle 1 in the cardiotoxicity group

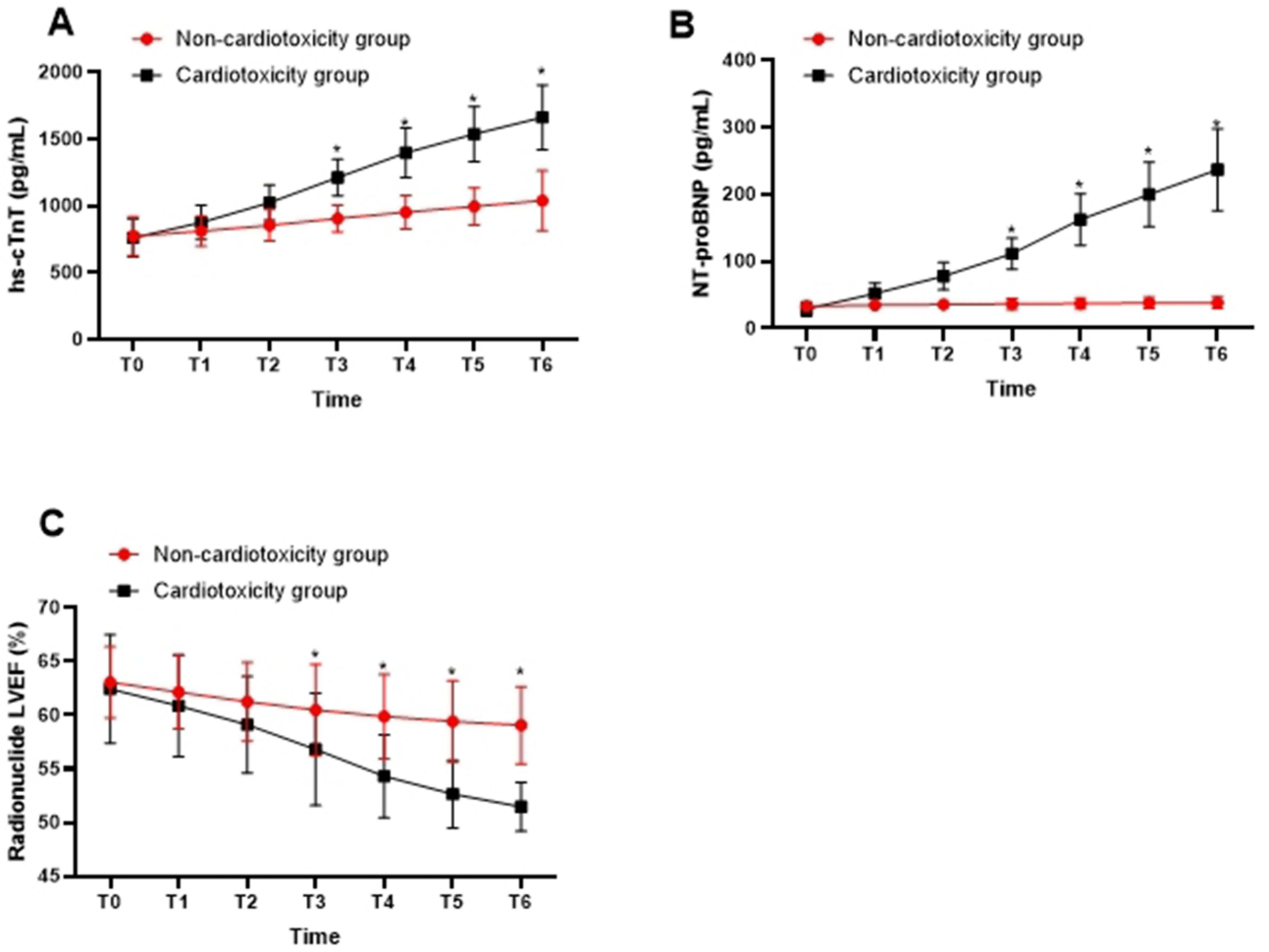

Figure 1 Serial changes in (**A**) hs-cTnI, (**B**) NT-proBNP, and (**C**) LVEF during six cycles of CEF chemotherapy. Data are mean ± SEM. The cardiotoxicity group is shown in black, the non-cardiotoxicity group in red. *P < 0.05 for intergroup comparison at the same time point.

reflects cumulative, subclinical cardiomyocyte damage. This pattern aligns with the seminal work by Cardinale et al, in which cTnI elevation following high-dose chemotherapy predicted subsequent left ventricular dysfunction months before the onset of symptoms or echocardiographic abnormalities, thereby offering a critical window for early intervention.[22] Unlike conventional markers such as CK-MB or LDH, hs-cTnI is unaffected by skeletal muscle injury, ensuring high cardiac specificity and enabling precise detection of anthracycline-mediated myocardial damage.

Pathophysiology of Anthracycline Cardiotoxicity and Correlation with Hs-cTnI

The kinetics of hs-cTnI elevation mirror the established dose-dependent mechanisms of anthracycline cardiotoxicity. Epirubicin, like other anthracyclines, induces cardiomyocyte apoptosis and necrosis primarily through oxidative stress and inhibition of topoisomerase IIβ, leading to irreversible structural injury.[23] The serial increase in hs-cTnI across chemotherapy cycles directly quantifies this cumulative myocyte loss. Our findings corroborate prior studies

Table 3 Multivariate Logistic Regression Analysis for Predictors of Cardiotoxicity

Variable	Adjusted Odds Ratio (aOR)	95% Confidence Interval (CI)	P
hs-cTnI at T_3 >1358.5 pg/mL	15.42	6.78–35.08	< 0.001
Age (per 1-year increase)	1.05	1.00–1.10	0.049

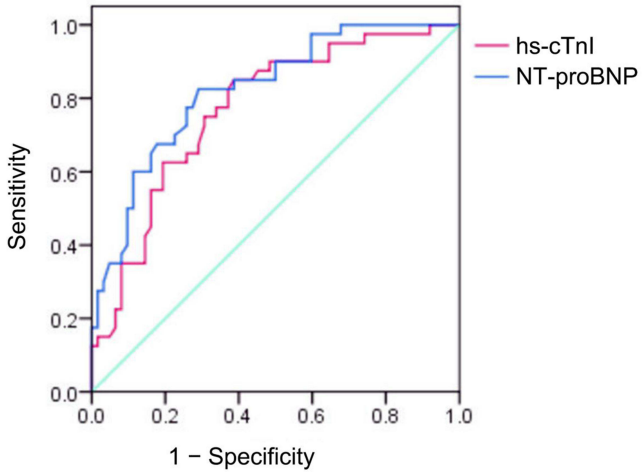

Figure 2 Receiver operating characteristic (ROC) curves for hs-cTnI and NT-proBNP at the third chemotherapy cycle (T_3). The area under the curve (AUC) for hs-cTnI (blue solid line) was 0.957, significantly higher than that for NT-proBNP (red solid line, AUC=0.684). The diagonal green line represents the line of no discrimination (AUC=0.5).

demonstrating a strong correlation between cumulative anthracycline dose and troponin release, with elevated levels predicting long-term cardiac dysfunction.[24] Although cyclophosphamide and 5-fluorouracil—components of the CEF regimen—can rarely cause acute cardiovascular toxicity, their contribution to chronic, progressive myocardial injury is minimal compared with epirubicin, as supported by contemporary cardio-oncology guidelines that categorize their cardiotoxic risk profiles differently.[25] The robust, dose-progressive association between hs-cTnI and the cumulative epirubicin dose (600 mg/m²), together with the drug's well-documented cardiotoxic profile, strongly supports epirubicin as the primary driver of the observed biomarker elevation and subsequent cardiac dysfunction.

Comparative Value of Hs-cTnI and NT-proBNP

The markedly lower predictive performance of NT-proBNP (AUC = 0.684) compared with hs-cTnI is physiologically plausible. NT-proBNP is a neurohormonal marker released in response to ventricular wall stress, volume overload, or hemodynamic compromise, and thus primarily reflects functional or structural ventricular remodeling rather than direct cellular injury.[26] In contrast, hs-cTnI serves as a direct indicator of cardiomyocyte damage. Our data illustrate this temporal hierarchy: hs-cTnI increased significantly as early as T_1, whereas a significant decline in LVEF emerged only at T_3, and NT-proBNP showed a delayed and moderate rise. This sequence—injury (cTnI) preceding systolic dysfunction (LVEF) and compensatory wall stress (NT-proBNP)—is consistent with prior prospective studies and explains the superior utility of hs-cTnI for early risk stratification.[27,28]

Clinical Implications and Future Directions

Our study identifies a clinically actionable threshold: an hs-cTnI level >1358.5 pg/mL at T_3 predicted cardiotoxicity with high sensitivity (92.0%) and specificity (91.5%). This suggests that a single mid-treatment biomarker assessment could efficiently stratify patients into risk categories. Those exceeding this threshold may benefit from intensified surveillance—including echocardiography with global longitudinal strain (GLS)—and should be considered for initiation of evidence-based cardioprotective therapy, such as ACEIs/ARBs or beta-blockers, in accordance with contemporary cardio-oncology guidelines.[29] Integrating serial hs-cTnI monitoring into routine oncology care may thus optimize the risk–benefit balance of essential anthracycline therapy. Future prospective trials should validate this cutoff in diverse populations and evaluate whether biomarker-guided cardioprotective strategies improve long-term cardiovascular outcomes.

Limitations

This study has several limitations. First, its single-center, retrospective design may introduce selection bias and limits generalizability despite balanced baseline characteristics. Second, all patients received a standardized CEF regimen with epirubicin (cumulative dose 600 mg/m²); therefore, our findings require validation in cohorts treated with other anthracyclines (eg, doxorubicin) or combination regimens, including HER2-targeted therapies or radiotherapy. Third, although LVEF was assessed at all timepoints by a single blinded cardiologist using the biplane Simpson's method per guideline recommendations, advanced echocardiographic parameters such as GLS—which may detect subclinical dysfunction earlier—were not routinely acquired during the study period (2021–2024) and thus unavailable for analysis. Fourth, incomplete documentation of baseline cardiovascular comorbidities and medications limits our ability to fully adjust for potential confounding effects of pre-existing conditions or cardioprotective drugs, a common constraint in retrospective analyses. Finally, the absence of long-term follow-up precludes assessment of whether early hs-cTnI elevation predicts late-onset heart failure or mortality.

Conclusion

In this retrospective cohort of postoperative breast cancer patients receiving a standardized CEF regimen, serial monitoring of high-sensitivity cardiac troponin I (hs-cTnI) proved to be a highly effective strategy for the early prediction of anthracycline-induced cardiotoxicity. hs-cTnI elevation occurred progressively from the first chemotherapy cycle, significantly preceded LVEF decline, and emerged as the strongest independent predictor of subsequent cardiac dysfunction. Specifically, an hs-cTnI concentration >1358.5 pg/mL after the third cycle identified high-risk patients with high diagnostic accuracy. In contrast, NT-proBNP demonstrated only moderate predictive value, underscoring its role as a downstream marker of ventricular stress rather than initial myocardial injury. These findings support the integration of dynamic hs-cTnI monitoring into clinical practice for early risk stratification. However, given the single-center design and regimen-specific context, these results should be regarded as hypothesis-generating. Definitive validation of hs-cTnI as a predictive tool requires larger, prospective, multicenter studies involving diverse anthracycline regimens and patient populations.

Disclosure

The authors declare that there is no conflict of interest regarding the publication of this paper.

References

1. Wang W, Sun Y, Li J, et al. Global, regional, and national burden of breast cancer in young women from 1990 to 2021: findings from the global burden of disease study 2021. *BMC Cancer*. 2025;25(1):1015. doi:10.1186/s12885-025-14416-1
2. Zhang T, Sun S, Xia T, et al. Trends in breast cancer mortality attributable to metabolic risks in Chinese women from 1990 to 2019: an age-period-cohort analysis. *Front Oncol*. 2024;14:1369027. doi:10.3389/fonc.2024.1369027
3. Sorodoc V, Sirbu O, Lionte C, et al. The value of troponin as a biomarker of chemotherapy-induced cardiotoxicity. *Life*. 2022;12(8):1183. doi:10.3390/life12081183
4. Simoes R, Silva LM, de Oliveira AN, et al. Identification of clinical and laboratory variables associated with cardiotoxicity events due to doxorubicin in breast cancer patients: a 1-year follow-up study. *Cardiovasc Toxicol*. 2021;21(2):106–114. doi:10.1007/s12012-020-09600-7
5. Silva EN, Ribeiro ML, Caldeira LC, et al. Biomarkers and prediction of anthracyclic cardiotoxicity in breast cancer. *Revista da Associacao Medica Brasileira*. 2024;70(suppl 1):e2024S106. doi:10.1590/1806-9282.2024S106
6. Serrano JM, Mata R, González I, et al. Early and late onset cardiotoxicity following anthracycline-based chemotherapy in breast cancer patients: incidence and predictors. *Int J Cardiol*. 2023;382:52–59. doi:10.1016/j.ijcard.2023.04.026
7. Semeraro GC, Cipolla CM, Cardinale DMJC. Role of cardiac biomarkers in cancer patients. *Cancers*. 2021;13(21):5426.
8. Sandamali JAN, Hewawasam RP, Fernando MA, Jayatilaka KA. Electrocardiographic and biochemical analysis of anthracycline induced cardiotoxicity in breast cancer patients from Southern Sri Lanka. *BMC Cancer*. 2023;23(1):210.
9. Prasad K, Yadav BS, Zohmangaihi D, Ballari N, Mehrotra S. Evaluation of anthracycline-induced cardiotoxicity using cardiac biomarkers: a prospective study. *Ind J Cancer*. 2024;2024:10–4103.
10. Montisci A, Palmieri V, Liu JE, et al. Severe cardiac toxicity induced by cancer therapies requiring intensive care unit admission. *Front Cardiovasc Med*. 2021;8:713694. doi:10.3389/fcvm.2021.713694
11. Mauro C, Capone V, Cocchia R, et al. Cardiovascular side effects of anthracyclines and HER2 inhibitors among patients with breast cancer: a multidisciplinary stepwise approach for prevention, early detection, and treatment. *J Clin Med*. 2023;12(6):2121. doi:10.3390/jcm12062121
12. Abdel-Salam O ME, Baset M Abd, Omara EA, Sleem AA. Protection by L-arginine Against Epinephrine-induced Arrhythmia and Cardiotoxicity. *Innov Discov*. 2024;1(2):12. doi:10.53964/id.2024012
13. Mabudian L, Jordan JH, Bottinor W, et al. Cardiac MRI assessment of anthracycline-induced cardiotoxicity. *Front Cardiovasc Med*. 2022;9:903719. doi:10.3389/fcvm.2022.903719

14. Drafts BC, Twomley KM, D'Agostino R, et al. Low to moderate dose anthracycline-based chemotherapy is associated with early noninvasive imaging evidence of subclinical cardiovascular disease. *JACC*. 2013;6(8):877–885. doi:10.1016/j.jcmg.2012.11.017
15. Lyon AR, Lopez-Fernandez T, Couch LS, et al. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS) Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC). *Eur Heart J Cardiovasc Imaging*. 2022;23(10):e333–e465. doi:10.1093/ehjci/jeac106
16. Michel L, Mincu RI, Mahabadi AA, et al. Troponins and brain natriuretic peptides for the prediction of cardiotoxicity in cancer patients: a meta-analysis. *Eur J Heart Failure*. 2020;22(2):350–361. doi:10.1002/ejhf.1631
17. Ndzie Noah ML, Nath ND, Yoshioka J. Chemotherapy-induced cardiotoxicity in breast cancer: mechanisms, diagnostic advances, and emerging protective strategies. *Am J Physiol Heart Circul Physiol*. 2025;329(6):H1508–H1525. doi:10.1152/ajpheart.00377.2025
18. Zamorano JL, Lancellotti P, Rodriguez Munoz D, et al. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: the Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). *Eur Heart J*. 2016;37(36):2768–2801. doi:10.1093/eurheartj/ehw211
19. Hahn RT, Saric M, Faletra FF, et al. Recommended standards for the performance of transesophageal echocardiographic screening for structural heart intervention: from the American Society of Echocardiography. *J Am Soc Echocardiograph*. 2022;35(1):1–76. doi:10.1016/j.echo.2021.07.006
20. Keihanian S, Ghaffari F, Fotokian Z, et al. The efficacy of biomarkers indexes in comparison with Echocardiography in assessment of antracycline induced cardiotoxicity in cancer patients. *J Inflamm Dis*. 2010;13(4):5–11.
21. Sugiura T, Nawaz S, Ferrell BE, Yoshida T. Induced Pluripotent Stem Cells: A New Dawn for the Treatment of Ischemic Cardiomyopathy. *Innov Discov*. 2024;1(4):31. doi:10.53964/id.2024031
22. Hutchins E, Yang EH, Stein-Merlob AFJCCR. Inflammation in chemotherapy-induced cardiotoxicity. *Current Cardiol Rep*. 2024;26(12):1329–1340. doi:10.1007/s11886-024-02131-5
23. Gavila J, Seguí MÁ, Calvo L, et al. Evaluation and management of chemotherapy-induced cardiotoxicity in breast cancer: a Delphi study. *Clin Transl Oncol*. 2017;19(1):91–104. doi:10.1007/s12094-016-1508-y
24. Díaz-Antón B, Madurga R, Zorita B, et al. Early detection of anthracycline- and trastuzumab-induced cardiotoxicity: value and optimal timing of serum biomarkers and echocardiographic parameters. *ESC Heart Fail*. 2022;9(2):1127–1137. doi:10.1002/ehf2.13782
25. Caballero RM, Antolín JM, Hernández RM, et al. Incidence of long-term cardiotoxicity and evolution of the systolic function in patients with breast cancer treated with anthracyclines. *Cardiol J*. 2022;29(2):228–234.
26. Balaji S, Antony AK, Tonchev H, et al. Racial disparity in anthracycline-induced cardiotoxicity in breast cancer patients. *Biomedicines*. 2023;11(8):2286. doi:10.3390/biomedicines11082286
27. Alexandraki A, Papageorgiou E, Zacharia M, et al. New insights in the era of clinical biomarkers as potential predictors of systemic therapy-induced cardiotoxicity in women with breast cancer: a systematic review. *Cancers*. 2023;15(13):3290. doi:10.3390/cancers15133290
28. Ahmed NA, Redwan FN, Jahjah AS, Al-Shehabi ZA. Evaluating high-sensitivity cardiac troponin I for early detection of treatment-related cardiotoxicity in HER2-positive breast cancer patients. *Annals Med Surg*. 2025;87(1):93–102.
29. Varghese S. EXercise to prevent AnthraCycline-based Cardio-Toxicity (EXACT 2.0) in women with breast cancer. 2021.