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Assessing the Impact of Combined Analyses of Cardiac N-Terminal Pro-Brain Natriuretic Peptide and Global Longitudinal Strain for Early Detection of Breast Cancer Cardiotoxicity

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ABSTRACT

Background: Advances in cancer treatment have improved survival rates, but cardiovascular complications remain a concern, necessitating early detection of chemotherapy-induced cardiotoxicity. Transthoracic echocardiography, mainly left ventricular ejection fraction (LVEF), is the standard assessment tool, though it often detects later-stage dysfunction. Global longitudinal strain (GLS) offers greater sensitivity, and cardiac biomarkers like NT-pro BNP provide additional prognostic value. Current guidelines emphasize biomarker monitoring over imaging in low cardiovascular (CV) risk patients. This study evaluates the combined use of NT-pro BNP levels and left and right ventricular longitudinal strain (LVGLS and RVFWLS) for early cardiotoxicity detection in breast cancer patients receiving anthracycline therapy.

Objectives: Our study aimed to evaluate the effectiveness of combined analyses of serum Cardiac N Terminal Pro Brain Natriuretic Peptide (NT-pro BNP) levels and global longitudinal strain (left ventricular global longitudinal strain (LVGLS)and right ventricular free wall longitudinal strain (RVFWLS)) in the early detection of chemotherapy-induced cardiotoxicity in low cardiovascular (CV) risk breast cancer patients receiving anthracycline therapy.

Methods: A cohort of 22 female breast cancer patients receiving anthracycline chemotherapy underwent baseline and follow-up assessments, including echocardiographic parameters and NT-pro BNP measurements. Changes in longitudinal strain >15% and NT-pro BNP levels (>125pg/ml) were analyzed, along with their correlation.

Results: NT-pro BNP concentration increased in 59% of cases post-chemotherapy. While left ventricle ejection fraction (LVEF) remained stable, there was a significant decrease in LVGLS -19.8±4.9 to -17.1 ± 6.0 (t-test=-3.06, df=21, p=0.006). Also, RVFWLS declined from -22.3±4.4 to -19.0 ± 4.6 (t-test=-2.85, df=21, p=0.010). Multivariate regression analyses revealed a joint effect of LVGLS and RVFWLS on changes in NT-pro BNP levels. RVFWLS showed potential as a subtle indicator of subclinical cardiotoxicity.

Conclusions: The combined assessment of NT-pro BNP levels and both left and right ventricular longitudinal strains (LVGLS and RVFWLS) demonstrates potential as an effective strategy for early detection of chemotherapy-induced cardiotoxicity in breast cancer patients with low cardiovascular risk. Specifically, RVFWLS may serve as a sensitive indicator of subclinical cardiotoxicity. However, larger-scale studies with extended follow-ups are necessary to confirm these findings, refine risk assessment, and enhance monitoring protocols in cardio-oncology.

Keywords: Anthracycline chemotherapy; breast cancer; cardiac biomarker NT-pro BNP; cardiotoxicity; cardio-oncology; global longitudinal strain.

BACKGROUND

The advent of innovative cancer treatments has significantly enhanced the chances of survival for individuals with cancer.[1] The field of cardio-oncology has arisen due to cardiovascular complications associated with a broad spectrum of therapeutic approaches.[2,3] Risk stratification before chemotherapy and early detection of subclinical cardiotoxicity are the keys in patients treated with chemotherapy. Transthoracic echocardiography stands as the preferred imaging modality for baseline risk assessment. It remains the primary tool for detecting left ventricle (LV) dysfunction, with a focus on accurately measuring left ventricular ejection fraction (LVEF).[4,5] However, relying on conventional measurements allows for the identification of cardiac dysfunction only at a later stage, and by that time, the damage may already be irreversible.[6,7] Therefore, it is crucial to identify accurate and reproducible measures capable of detecting early subtle changes.[4,8] Global longitudinal strain (GLS) has demonstrated efficacy as a robust predictor of cardiac dysfunction in various diseases and is a reliable marker of cardiotoxicity.[9] Cardiac biomarkers play an essential role in detecting cardiotoxicity, aiding in guiding ongoing cancer therapy to improve overall cancer survival. They also help complement imaging during treatment to detect subclinical disease more effectively.[10,11] However, the association between elevated basal cardiac N terminal pro-brain Natriuretic Peptide (NT-pro BNP) levels and increased risk of cardiotoxicity remains unknown, though it suggests a potentially worse prognosis.[12] The frequency of cardiac imaging monitoring during therapy should be adjusted according to the estimated baseline risk, the type of drug, the treatment setting, and the combination with other therapies.[13] Even though combining GLS with cardiac biomarkers has been suggested to enhance diagnostic accuracy for early cardiotoxicity detection, the latest cardio-oncologic guidelines recommend measuring peptide levels more frequently than imaging diagnostic tools in low cardiovascular (CV) risk

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patients.[14] Therefore, our study aimed to evaluate the effectiveness of the combined analyses of serum cardiac peptide NT-pro BNP levels and global longitudinal strain (left ventricular longitudinal strain (LVGLS), right ventricular free wall longitudinal strain (RVFWLS), emphasizing the additional role of right ventricular strain analyses in the early detection of chemotherapy-induced cardiotoxicity, in low CV risk breast cancer patients receiving anthracycline therapy.

METHODS

Inclusion and exclusion criteria

This study included female patients over 18 years old with newly diagnosed breast cancer who were scheduled to receive chemotherapy. Exclusion criteria were as follows: patients who declined to participate in the trial, those with a pre-existing diagnosis of coronary artery disease (CAD) or heart failure (HF) (defined as left ventricular ejection fraction [LVEF] <55%), and those who had undergone chemotherapy previously.

The study population

Women with breast cancer were evaluated based on the HFA-ICOS risk assessment, which considers cardiovascular (CV) risk factors, cardiovascular disease (CVD) history, cancer history, and cancer treatment history. A total of 44 patients with low cardiovascular risk factors who had planned breast cancer treatment were prospectively included in this single-center study between June 2022 and August 2023. However, the eligible study population was inherently limited due to the strict inclusion criteria focusing on low cardiovascular (CV) risk patients. Additionally, eleven patients were excluded due to poor 2D image quality, changing hospitals, or failure to attend the second visit on time. Consequently, 33 patients were enrolled in the trial. Only 22 patients receiving anthracycline therapy met the study's objective and were analyzed accordingly. The restricted sample size reflects the stringent selection criteria required to maintain a homogeneous population and ensure the accuracy of the study's findings.

All participants provided written informed consent before being included in the trial. The study also received ethics approval from the relevant ethics committee, ensuring compliance with ethical standards.

Baseline (T0) and post-treatment (follow-up) (T1) assessments included demographic data, electrocardiogram (ECG), echocardiographic parameters, and cardiac biomarkers (natriuretic peptide: NT-pro BNP).

Chemotherapy regimen

The patients received either doxorubicin at 60 mg/m² or epirubicin at 100 mg/m², along with cyclophosphamide at 600 mg intravenously, administered in 21-day cycles.

Standard echocardiographic data

All patients underwent standard transthoracic 2D echocardiography during the initial and follow-up visits using a GE Vivid E9 ultrasound machine (GE Healthcare, Horten, Norway) with an M5S (1.7-3.3 MHz) transducer, adhering to the guidelines of the American Society of Echocardiography (ASE). Echocardiographic images were acquired at an average of 70-90 frames per second and digitally stored for three cardiac cycles.

Speckle tracking echocardiography (STE)

STE analyses were performed following the American Society of Echocardiography guidelines. All patients were in sinus rhythm. For the left ventricle (LV), the peak-systolic strain was automatically calculated from the mean of the six traced segments for each 2D apical view (two-, three-, and four-chamber). LV global longitudinal strain (GLS) was calculated by averaging the peak-systolic strain of the apical views. Right ventricular free wall strain (RVFWLS) was calculated using the standard RV-focused apical four-chamber view. A relative decline in GLS by more than 15% from baseline was considered indicative of chemotherapy-induced cardiovascular toxicity (CTR-CVT). The tracking quality was visually validated, and segments that did not initially track correctly were manually adjusted. Segments that could not be tracked correctly after manual adjustment were excluded. Images with poor quality that precluded speckle analysis in two or more consecutive segments were also excluded.

Biomarkers

NT-pro BNP concentrations were measured using a commercially available chemiluminescence immunoassay on a Snibe Maglumi 800 analyzer. NT-pro BNP levels exceeding 125 pg/mL were deemed elevated by the 99th percentile reference limit. Blood samples were analyzed at baseline (T0) and follow-up (T1) time points.

Statistical analysis

Statistical analyses were conducted using the Statistical Program for Social Science (SPSS) version 23.0 software package (IBM SPSS, Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation (SD). All statistical tests were two-sided t-tests. Multiple regression analyses were performed to assess the collective effect of various factors (independent variables: age, BMI, etc.) on the outcome variables NT-pro BNP, LVGLS, and RVFWLS of all 33 patients. Correlation analysis was performed using the Pearson correlation coefficient. P-values less than 0.05 were considered statistically significant.

RESULTS

Our sample included 22 female patients with an average age of 46.7±13.0 years. Baseline characteristics are provided in Table 1. Patients received neoadjuvant treatment before surgery, and their follow-up visits were scheduled at the end of the fourth cycle, following the cumulative anthracycline dosage.

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Thirteen patients were treated with doxorubicin, with a mean cumulative dosage of 431±38 mg/m², while nine patients received epirubicin at a cumulative dosage of 666±75 mg/m². Most patients were at stages 2 and 3 (27% and 24%, respectively), with 15% at stage 1.

TABLE 1. Baseline clinical characteristics of the study patients (n=22)

Variables	Values	Median (Min, Max)
Age (years)	46.7 (13.0)	44.0 (30.0, 73.0)
Diabetes melitus, n (%)	1 (4.5%)	-
Arterial hypertension, n (%)	4 (18.2%)	-
Systolic BP, mmHg, mean (SD)	119.2 (18.6)	115.0 (90.0, 160.0)
Diastolic BP, mmHg, mean (SD)	77.0 (10.9)	77.0 (60.0, 100.0)
Heart rate, BPM, mean (SD)	75.2 (9.8)	75.0 (60.0, 90.0)
Creatinine, umol/L, mean, (SD)	76.9 (10.0)	77.0 (58.0, 90.0)
GFR, mL/min/1.73 m², mean, (SD)	91.9 (17.0)	93.0 (69.0, 130.0)
No smoking history, n (%)	22 (100%)	-
No alcohol consumption, n (%)	22 (100%)	-
NT pro-BNP, pg/mL, mean, SD	89.8 (65.2)	72.4 (10.0, 290.0)
Weight, kg, mean (SD)	78.6 (22.3)	70.0 (47.0, 135.0)
Height, cm, mean (SD)	161.1 (5.3)	161.0 (150.0, 172.0)
Body Mass Index, kg/m², mean (SD)	29.9 (7.5)	28.6 (18.6, 46.1)
LVEF, %, mean (SD)	64.6 (3.7)	65.0 (58.0, 76.0)
Left Ventricle GLS (LVGLS), mean (SD)	-19.8 (4.9)	-20.7 (-25.1, -16.0)
Right Ventricle GLS (RVFWLS), mean (SD)	-22.3 (4.4)	-22.3 (-30.8, -15.3)
TAPSE, mm, mean (SD)	24.8 (3.3)	24.0 (20.0, 33.0)

Explanations and abbreviations: Continuous data is expressed as mean ± SD. BMI, body mass index; BP, blood pressure; GFR, glomerular filtration rate; Hyphens (-), no data is applicable; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; NT-pro BNP, N-terminal pro-b-type natriuretic peptide; RVFWLS, right ventricular free wall longitudinal strain; TAPSE, tricuspid annular plane systolic excursion.

During the follow-up visits, there were no significant changes in the left ventricular ejection fraction (LVEF) after the chemotherapy treatment. The LVEF values remained unchanged from 64.6±3.7 to 65.0±3.0 (t-test=-0.40, df=21 and p= 0.693). Similarly, the analysis found insignificant changes in the values of tricuspid annular plane systolic excursion (TAPSE) after the chemotherapy treatment. The TAPSE values changed from 24.8±3.3 to 26.2±6.5 (t-test=-0.88, df=21 and p= 0.386).

Conversely, the study's findings indicated a significant reduction in left ventricular global longitudinal strain (LV-GLS) from baseline to the end of chemotherapy. The LV-GLS declined from -19.8±4.9 to -17.1±6.0 (t-test=-3.06, df = 21, p = 0.006). Likewise, the right ventricular free wall longitudinal strain (RVFWLS) fell from -22.3±4.4 to -19.0±4.6 (t-test=-2.85, df=21, p=0.010) (Tab.2).

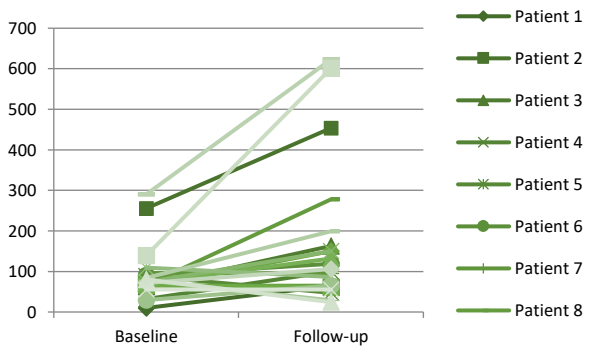
TABLE 2. Echocardiograpic parameters

Parameters	Baseline Mean (SD)	Follow-up Mean (SD)	Chi2 or paired t-test	df	p
VOT, mm	18 (1.2)	18.4 (1.4)	-0.33	21	0.747
Aortic Annulus, mm	21.7 (2.1)	21.8 (2.7)	-0.16	21	0.871
Sinus of Valsalva, mm	30.9 (5.5)	30.0 (3.6)	0.88	21	0.391
Sino tubular junction, mm	27.8 (3.6)	27.6 (3.2)	0.47	21	0.643
Asc. Aorta, mm	29.1 (3.3)	29.0 (3.1)	0.14	21	0.887
Des. Aorta, mm	20.7 (3.4)	21.4 (2.0)	-0.87	21	0.397
LA, mm	35.0 (2.9)	35.8 (2.5)	-1.12	21	0.277
IVSd, mm	9.4 (1.9)	9.6 (1.4)	-1.03	21	0.315
LVPWd, mm	9. 4 (1.7)	9.4 (1.4)	-0.16	21	0.877
LVEDd, mm	43.5 (4.6)	44.0 (4.0)	-0.48	21	0.633
RVEDd, mm	29.0 (3.5)	28.0 (2.9)	1.12	21	0.275
RA Minor, mm	34.0 (3.7)	33.4 (3.4)	0.74	21	0.465
RA Major, mm	40.8 (3.7)	40.4 (3.4)	0.31	21	0.757
IVC, mm	17.2 (1.3)	17.5 (1.2)	-0.86	21	0.398
Diastolic function					
-E	0.7 (0.2)	0.8 (0.2)	-0.83	21	0.416
-A	0.7 (0.2)	0.8 (0.2)	-0.83	21	0.494
-E/A	1.1 (0.3)	1.2 (0.5)	-1.73	21	0.098
-E/E'	8.1 (1.7)	5.1 (3.8)	3.43	21	0.003
Systolic function					
LVEF, %	64.6 (3.7)	65.0 (3.0)	-0.40	21	0.693
LVGLS	-19.8 (4.9)	-17.1 (6.0)	-3.06	21	0.006
RV FWLS	-22.3 (4.4)	-19.0 (4.6)	-2.85	21	0.010
TAPSE, mm	24.8 (3.3)	26.2 (6.5)	-0.88	21	0.386

Explanations and abbreviations: Data is expressed as mean ± SD. IVC, inferior vena cava; IVS, interventricular septal diameter; LA, left atria; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; LVPWd, left ventricle posterior wall diameter; RA, right atria; RVFWLS, right ventricular free wall longitudinal strain; TAPSE, tricuspid annular plane systolic excursion; VOT, ventricular outflow tract.

The mean value of the cardiac marker showed a statistically significant increase, rising from 89.8±65.2 pg/mL to 166.7±172.5 pg/mL (t-test=-2.84, df=21, p=0.010). However, this increase was observed in only 59.3% of cases. The NT-pro BNP concentration remained unchanged in 40.7% of cases (Fig.1).

FIGURE 1. Increase in NT-pro BNP. A scatter plot of the values changed for individual patients



In cases where the peptide levels remained constant, strain values decreased by more than 15%, with more patients experiencing changes in right ventricular free wall longitudinal

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strain (RVFWLS) compared to left ventricular global longitudinal strain (LVGLS).

Significant results were observed in a multiple regression analysis model encompassing the study population's clinical, echocardiographic, and ECG parameters. When assessing the changes in cardiac peptide levels (outcome variable: NT-proBNP), the independent variables LVGLS and RVFWLS, together with others, exhibited a noteworthy joint effect on the alteration in NT-pro BNP plasma levels (LVGLS beta-coefficient=8.96, p=0.028; RVFWLS beta-coefficient=-8.70, p=0.014) (Tab.3).

TABLE 3. Coefficients of regression, model outcome variable: NT-pro BNP

β coefficients	Unstandardized coefficients		Standardized coefficients	t-test	p	Correlation
	Value	SD				
Constant-β0	110.25	24.23	0.00	4.55	4.55	-
Delta_P wave	11.15	3.73	0.39	2.99	2.99	Positive
Delta_PR interval	-5.82	1.68	-0.47	-3.48	-3.48	Negative
Delta_Aor.Ann.	-23.21	6.77	-0.38	-3.43	-3.43	Negative
Delta_Sinn.Valsalva	8.10	3.88	0.21	2.12	2.12	Positive
Delta_Sinotubular Junction	28.10	5.64	0.52	4.98	4.98	Positive
Delta_LA	11.41	4.97	0.25	2.29	2.29	Positive
Delta_IVSD	-58.89	11.54	-0.59	2.24	2.24	Negative
Delta_LVEDd	-18.94	3.19	-0.62	-5.11	-5.11	Negative
Delta E/A	-84.04	37.21	-0.27	-5.94	-5.94	Negative
Delta_LVEF	14.02	5.39	0.30	-2.26	-2.26	Positive
Delta_LVGLS	8.96	3.77	0.24	2.60	2.60	Positive

Explanations and abbreviations: Hyphens (-), no data is applicable; IVSD, interventricular septal diameter; LA, left atrium; LVEDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; RVFWLS, right ventricular free wall longitudinal strain. The model showed a highly significant joint effect of the parameters included in the model on the outcome variable - the change of NT pro-BNP (F-test=8.27, p<0.001).

LVGLS changes, NT-pro BNP plasma levels with other variables displayed a significant effect (NT-pro BNP - beta-coefficient=0.02, p<0.001) (Tab.4).

TABLE 4. Coefficients of regression, model outcome variable: LVGLS

β coefficients	Unstandardized coefficients		Standardized coefficients	t-test	p	Correlation
	Value	SD				
Constant-β0	1.39	0.57	0.00	2.43	0.022	-
Delta_NT-pro BNP	0.02	0.00	0.57	4.22	0.000	Positive
Delta_QTc	-0.16	0.03	-0.78	-5.03	0.000	Negative
Delta_AA	0.66	0.21	0.40	3.07	0.005	Positive
Delta_SV	-0.63	0.15	-0.62	-4.18	0.000	Negative
Delta_LA	0.28	0.13	0.28	2.14	0.042	Positive
Delta_LVEF	-0.63	0.18	-0.50	-3.59	0.001	Negative

Explanations and abbreviations: AA, aortic annulus; Hyphens (-), no data is applicable; LA, left atrium; LVEF, left ventricular ejection fraction; NT-pro BNP, N-terminal pro-b-type natriuretic peptide; QTc, corrected QT interval; SV, sinus of Valsalva. The model showed a highly significant joint effect of the changes of the parameters included in the model on the outcome variable - the change of LVGLS (F-test=6.67, p<0.001).

However, when assessing the changes of RVFWLS, the changes of NT-pro BNP plasma levels with other variables showed a moderately significant effect (NT-pro BNP beta-coefficient=-0.02, p=0.006) (Tab.5)

TABLE 5. Coefficients of regression, model outcome variable: RVFWLS

β coefficients	Unstandardized coefficients		Standardized coefficients	t-test	p	Correlation
	Value	SD				
Constant-β0	5.84	1.16	0.00	5.05	0.000	(-)
Delta_NT-proBNP	-0.02	0.01	-0.52	-2.97	0.006	Negative
Delta_Ass. Aorta	0.70	0.26	0.43	2.76	0.010	Positive
Delta_IVSD	1.86	0.76	0.61	2.44	0.022	Positive
Delta_LVPWD	-2.17	0.79	-0.70	-2.74	0.011	Negative
Delta_E	-7.48	2.91	-0.42	-2.57	0.016	Negative
Delta_E/e'	0.58	0.23	0.48	2.52	0.018	Positive

Explanations and abbreviations: Ass. aorta, ascending aorta; Hyphens (-), no data is applicable; IVSD, interventricular septal diameter; LVPWD, left ventricular posterior wall diameter; NT-pro BNP, N-terminal pro-b-type natriuretic peptide. The model showed a highly significant joint effect of the changes of the parameters included in the model on the outcome variable - the change of RVFWLS (F-test=3.34, p=0.014).

DISCUSSION

Over the past decade, the increase in cancer survivorship has heightened concerns about cardiac health due to cardiotoxicity induced by cancer treatments. The latest cardio-oncology guidelines recommend baseline cardiotoxicity risk stratification. Classifying patients based on their risk of anthracycline-induced cardiovascular toxicity has enabled the early application of personalized preventive strategies. For low-risk patients receiving anthracycline, the surveillance protocol suggests more frequent measurement of cardiac serum biomarkers rather than relying heavily on imaging modalities.[5]

Our study aimed to evaluate the combined predictive role of NT-proBNP and ventricular longitudinal strain, assessing the additional role and preference of imaging techniques for detecting subclinical cardiotoxicity following the cumulative dose of anthracycline in low-risk patients. Results indicate that the increase in serum cardiac levels was significant in more than half of the cases. Furthermore, in 45% of these cases, the peptide level increased above the reference limit (>125 pg/mL). However, when peptide levels remained unchanged (6/22), an RVFWLS decrease of more than 15% was observed in 50% of patients compared to LVGLS in 16%. This may suggest that RVFWLS may serve as a more subtle indicator of subclinical cardiotoxicity compared to LVGLS or cardiac peptide levels.

The existing literature on serum cardiac biomarkers for assessing CTR-CVT risk before cancer treatment is scarce, resulting in recommendations primarily based on expert consensus. Furthermore, there are no established cutoff values for cardiovascular biomarkers specific to cancer patients or those undergoing cancer therapy.[15] Among the instrumental diagnostic methods, longitudinal strain is an

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effective screening tool for risk assessment before cancer treatment and should be considered for all patients requiring baseline echocardiograms.[16-18] Various studies have explored the association between NT-pro BNP and left ventricular global longitudinal strain (LVGLS) as indicators of cardiotoxicity, yielding mixed results. Dong Y et al. determined that monitoring NT-pro BNP alongside echocardiography has clinical relevance, facilitating early detection of myocardial damage attributed to anthracyclines.[19] In a smaller study involving women with breast cancer receiving anthracycline treatment, elevated NT-pro BNP levels were noted in those who later developed cardiomyopathy.[20] Conversely, other researchers found no predictive value associated with NT-pro BNP levels.[21,22] Supporting our findings, Chang et al. highlighted the significance of right ventricular free wall longitudinal strain (RVFWLS) as a key measure for assessing concealed right ventricular (RV) dysfunction, with their results suggesting that RVFWLS could indicate a greater vulnerability to injury within the thinner RV wall. When examining studies focused on RV parameters, strain assessment appears to be the most beneficial for early prediction of the chemotherapy's effects on the right ventricle.[23] Oliveira et al. reported significant variations in the need for right ventricular assist devices among patients with chemotherapy-induced cardiomyopathy, particularly those treated with anthracycline, as opposed to other causes of cardiomyopathy (19% vs. 9.3%, $p < 0.0001$). This suggests that RV dysfunction will likely coincide with the more profound left ventricular dysfunction observed in this patient group.[24] Milano et al. demonstrated a decrease in both rights. The left ventricular thickness in mice treated with Doxorubicin or a combination of Doxorubicin and Trastuzumab, with both cohorts exhibiting increased RV-free wall fibrosis compared to the placebo or mice administered only Trastuzumab. This leads to the reasonable conclusion that chemotherapy might adversely affect RV structure and function in human patients.[25] These findings underscore the importance of incorporating RV strain analysis into cardiac monitoring strategies for chemotherapy patients, particularly for the early detection of RV dysfunction.

It is also essential to recognize that peptide measurements can be affected by age, weight, anemia, and renal function, making accurate interpretation challenging and potentially non-generalizable across all patient groups.[26]

Our study has several limitations. The first and most significant is the small sample size, which may limit the generalizability of our findings. Secondly, the short follow-up period may not capture long-term cardiotoxic effects. More significant, long-term studies are needed to further evaluate the detection of early signs of cardiotoxicity and the role of RVFWLS as a potential marker.

CONCLUSIONS

In conclusion, our study aimed to evaluate the combined predictive role of NT-pro BNP and GLS, underscoring the importance of the RVFWLS for detecting subclinical cardiotoxicity following anthracycline chemotherapy in low CV-risk breast cancer patients. Our findings highlight several key points. First, a significant proportion of patients exhibited elevated NT-pro BNP levels after chemotherapy, indicating potential cardiotoxicity. Second, while conventional echocardiographic parameters such as LVEF remained stable, there was a significant decrease in LVGLS and RVFWLS, suggesting early subclinical cardiac dysfunction. Third, multivariate regression analyses showed that LVGLS and RVFWLS had a significant joint effect on changes in NT-pro BNP levels, emphasizing their combined predictive value. Fourth, our results suggest that RVFWLS may serve as a more subtle indicator of subclinical cardiotoxicity than LVGLS or cardiac peptide levels. Finally, we underscore the importance of including RV strain analysis in cardiac monitoring protocols for chemotherapy patients to detect early signs of cardiotoxicity.

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