

Original Article

Global longitudinal strain and left ventricular ejection fraction for early detection of chemotherapy-related cardiac dysfunction in breast cancer: A prospective comparison of doxorubicin-based and paclitaxel–carboplatin regimens

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Abstract

Left ventricular ejection fraction (LVEF) is widely used in routine practice to assess cardiotoxicity; however, reductions in LVEF often reflect relatively advanced myocardial damage. Global longitudinal strain (GLS) quantifies myocardial deformation and has demonstrated greater sensitivity for identifying early systolic dysfunction, yet comparative evidence on myocardial strain changes between doxorubicin-based regimens and non-anthracycline chemotherapy in breast cancer patients remains limited. The aim of this study was to compare changes in left ventricular GLS and LVEF between breast cancer patients receiving doxorubicin-based chemotherapy and those treated with paclitaxel–carboplatin regimens. A prospective cohort study was conducted among 106 women with histopathologically confirmed breast cancer, who were allocated to receive either a doxorubicin-based regimen (n=53) or a paclitaxel–carboplatin regimen (n=53). Transthoracic echocardiography was performed within seven days before chemotherapy initiation and repeated after four months. Left ventricular GLS was measured using two-dimensional speckle-tracking echocardiography from apical views and analyzed offline using the 17-segment model. Baseline GLS values did not differ significantly between the doxorubicin and paclitaxel–carboplatin groups (-20.47 ± 0.45 vs -20.38 ± 0.53 ; $p=0.410$). After four months, GLS was significantly reduced in the doxorubicin group compared with the paclitaxel–carboplatin group (-15.04 ± 0.35 vs -19.54 ± 0.50 ; $p<0.001$). The change in GLS (Δ GLS) was also greater in the doxorubicin group (5.43 ± 0.12 vs 0.84 ± 0.11 ; $p<0.001$). No significant differences were observed in LVEF before chemotherapy (55.26 ± 1.78 vs 55.39 ± 1.99 ; $p=0.720$), after chemotherapy (51.32 ± 1.51 vs 51.60 ± 1.64 ; $p=0.359$), or in Δ LVEF ($p=0.484$). In conclusion, doxorubicin-based chemotherapy was associated with early subclinical systolic dysfunction detectable by GLS before measurable LVEF decline, whereas paclitaxel–carboplatin was associated with relatively preserved myocardial deformation. These findings support the incorporation of strain imaging into routine cardiac surveillance for earlier identification and management of chemotherapy-related myocardial injury.

Keywords: Breast cancer, doxorubicin, cardiotoxicity, global longitudinal strain, cancer therapy–related cardiac dysfunction



Introduction

Cancer remains a major global health challenge and a leading cause of death worldwide [1]. In 2022, an estimated 9.6 million deaths were attributed to malignancy, positioning cancer as the second most common cause of mortality after cardiovascular diseases [2]. Cancer incidence continues to rise, with projections indicating that by 2040, annual cases may exceed 3 million, accompanied by nearly 1 million deaths, largely driven by population growth and ageing [3]. Breast cancer is the most frequently diagnosed malignancy among women and contributes significantly to cancer-related morbidity and mortality, particularly in regions where diagnosis often occurs at an advanced stage [4].

Therapeutic advances have improved survival in breast cancer; however, these gains are increasingly tempered by treatment-related cardiovascular toxicity [5,6]. Cancer therapy-related cardiac dysfunction (CTRCD) has emerged as a clinically relevant complication, especially in patients exposed to anthracyclines, a class of cytotoxic antineoplastic antibiotics commonly used in cancer chemotherapy [7]. Doxorubicin, a key component of many breast cancer regimens, is associated with cumulative dose-dependent myocardial injury [8]. Structural and functional alterations may progress silently before manifesting as symptomatic heart failure [9]. As survivorship improves, prevention and early detection of cardiotoxicity have become integral to comprehensive oncologic care.

Echocardiography remains the cornerstone for cardiac surveillance in patients receiving potentially cardiotoxic therapy [10]. Left ventricular ejection fraction (LVEF) is widely used in routine practice; however, reductions in LVEF often reflect relatively advanced myocardial damage [7]. Subclinical impairment may precede measurable changes in LVEF, limiting its sensitivity for early detection [9]. Global longitudinal strain (GLS), derived from speckle-tracking echocardiography, quantifies myocardial deformation and has demonstrated superior sensitivity in identifying early systolic dysfunction [8]. A relative decline in GLS has been associated with the subsequent development of CTRCD, even when LVEF remains within normal limits [11].

GLS enables early detection of subclinical myocardial dysfunction in patients undergoing chemotherapy, preceding clinically significant reductions in LVEF [8]. GLS analysis also provides additional information on myocardial deformation and allows assessment of tracking quality, which may improve the reliability of myocardial function evaluation when image acquisition and analysis are performed appropriately. These features position GLS as a sensitive imaging parameter with added value for the surveillance of chemotherapy-induced cardiotoxicity. The aim of this study was to evaluate differences in left ventricular GLS and LVEF between patients receiving doxorubicin-based chemotherapy and those treated with paclitaxel-carboplatin regimens. To the best of our knowledge, this is the first study conducted in Indonesia to compare GLS changes across these chemotherapy regimens, providing initial regional data on the role of GLS as an early marker of cardiotoxicity in patients with breast cancer.

Methods

Study design and setting

A prospective cohort study was conducted from August to December 2025 at a tertiary referral center, Dr. Zainoel Abidin Hospital, in Banda Aceh, Indonesia, enrolling consecutive women aged 18–69 years with histopathologically confirmed breast cancer who received first-line doxorubicin-based or paclitaxel-carboplatin chemotherapy. Transthoracic echocardiography was performed within seven days before chemotherapy initiation and repeated after four months. Left ventricular GLS was assessed using two-dimensional speckle-tracking echocardiography and analyzed offline using the 17-segment model.

Sample size and sampling method

Sample size was estimated for a two-group comparison of means using a clinically relevant effect size, defined a priori as a 10–15% relative reduction in GLS, consistent with subclinical myocardial dysfunction. Assuming a baseline GLS of approximately -20 and a standard deviation of 3, a 10% relative change corresponds to an absolute difference of 2. With a two-sided α of 0.05

and 80% power, the minimum required sample size was 35 patients per group. Allowing for an anticipated 10% attrition, the minimum target enrolment was increased to 39 patients per group. Consecutive sampling was applied, and all eligible patients during the study period were enrolled.

Patients and eligibility criteria

Eligible participants were women aged ≥ 18 and < 70 years with histopathologically confirmed breast cancer who were scheduled to receive first-line chemotherapy with either a doxorubicin-based regimen or a paclitaxel–carboplatin combination. Participants were also required to have complete baseline and follow-up echocardiographic data. Patients were excluded if they had baseline LVEF $< 55\%$ or abnormal baseline GLS, acute coronary syndrome, or severe arrhythmias, including ventricular arrhythmia, ventricular fibrillation, or second-degree or complete atrioventricular block requiring pacemaker implantation. Additional exclusion criteria were moderate-to-severe valvular disease, prosthetic heart valves, congenital heart disease, severe comorbid conditions that could affect echocardiographic assessment, such as advanced chronic kidney disease or terminal-stage malignancy, sepsis, inadequate echocardiographic image quality, including poor acoustic window or unsatisfactory myocardial tracking, and refusal to provide written informed consent.

Data collection

Demographic and clinical data were collected at enrollment using a standardized data extraction form. Demographic variables included age and sex, while clinical variables included cancer type, chemotherapy regimen, cumulative chemotherapy dose, baseline blood pressure, body mass index (BMI), and relevant comorbid conditions. Data were obtained from electronic and paper-based medical records, oncology treatment records, and direct clinical evaluation at the time of recruitment. Chemotherapy regimens, dosing schedules, and cumulative doses were systematically verified using oncology treatment records. All data extraction was conducted by a single trained investigator. To ensure data accuracy, entries were cross-checked against source documents, and any inconsistencies were resolved through repeated review of the original records.

Measurement of global longitudinal strain (GLS)

Baseline transthoracic echocardiography was performed within seven days prior to initiation of the first chemotherapy cycle. Follow-up echocardiographic evaluation was conducted after four months of chemotherapy initiation, whichever occurred first, in accordance with institutional cardiac monitoring practice. All examinations were performed by an experienced cardiologist blinded to the chemotherapy regimen. Echocardiographic examinations were conducted using a commercially available ultrasound system equipped with a 2.5–3.5 MHz phased-array transducer. Standard parasternal long-axis, parasternal short-axis, and apical views (four-chamber, two-chamber, and three-chamber) were acquired with patients positioned in the left lateral decubitus position. Digital cine loops were recorded at a frame rate of 50–80 frames per second for offline analysis. LVEF was calculated using the modified biplane Simpson method from apical four- and two-chamber views. Left ventricular GLS was measured using two-dimensional speckle-tracking echocardiography. Endocardial borders were manually delineated at end-systole, followed by automated myocardial tracking with manual adjustment when required to ensure optimal tracking quality. Longitudinal strain values from the standardized 17-segment model were averaged to obtain a global value. GLS was expressed as a percentage, with more negative values indicating better myocardial deformation. Only examinations with adequate image quality and satisfactory tracking in at least 16 of 17 segments were included in the final analysis.

Study variables

The primary independent variable was the chemotherapy regimen, categorized into two groups: (1) doxorubicin-based regimen and (2) paclitaxel–carboplatin regimen. A doxorubicin-based regimen was defined as any chemotherapy protocol containing doxorubicin, classified as a type I cardiotoxic agent, administered as monotherapy. The paclitaxel–carboplatin regimen was defined as a first-line, non-anthracycline chemotherapy protocol consisting of paclitaxel (a

microtubule-stabilizing taxane agent) combined with carboplatin (a platinum-based alkylating agent), administered without concomitant exposure to anthracyclines or other agents. The primary dependent variable was left ventricular GLS and LVEF, measured at baseline (prior to chemotherapy initiation) and at follow-up after four months of chemotherapy initiation.

Statistical analysis

Statistical analysis was performed using SPSS version 25.0 (IBM Corp., Chicago, IL, USA) and GraphPad Prism version 10 (GraphPad Software, San Diego, CA, USA). Continuous variables were presented as mean \pm standard deviation or median (min–max) according to distribution, while categorical variables were expressed as frequencies and percentages. Between-group comparisons of GLS values were conducted using the student t-test for normally distributed data or the Mann–Whitney U test for non-normally distributed data. To further evaluate determinants of GLS, linear regression analysis was performed. Regression coefficients (β), standard errors (SE), and 95% confidence intervals (95%CI) were reported. A two-tailed $p < 0.05$ was considered statistically significant.

Results

Patient selection

A total of 153 patients with breast cancer were assessed at baseline (**Figure 1**). Patients were excluded due to acute coronary syndrome or severe arrhythmia ($n=1$) and incomplete medical records ($n=18$), resulting in 134 patients eligible for initial inclusion. During the 4-month follow-up period, 18 patients were lost to follow-up and 10 discontinued the chemotherapy, yielding a final analytic cohort of 106 patients. These patients were allocated into two groups according to chemotherapy regimen: doxorubicin ($n=53$) and paclitaxel–carboplatin ($n=53$). All patients who completed follow-up were included in the final analysis.

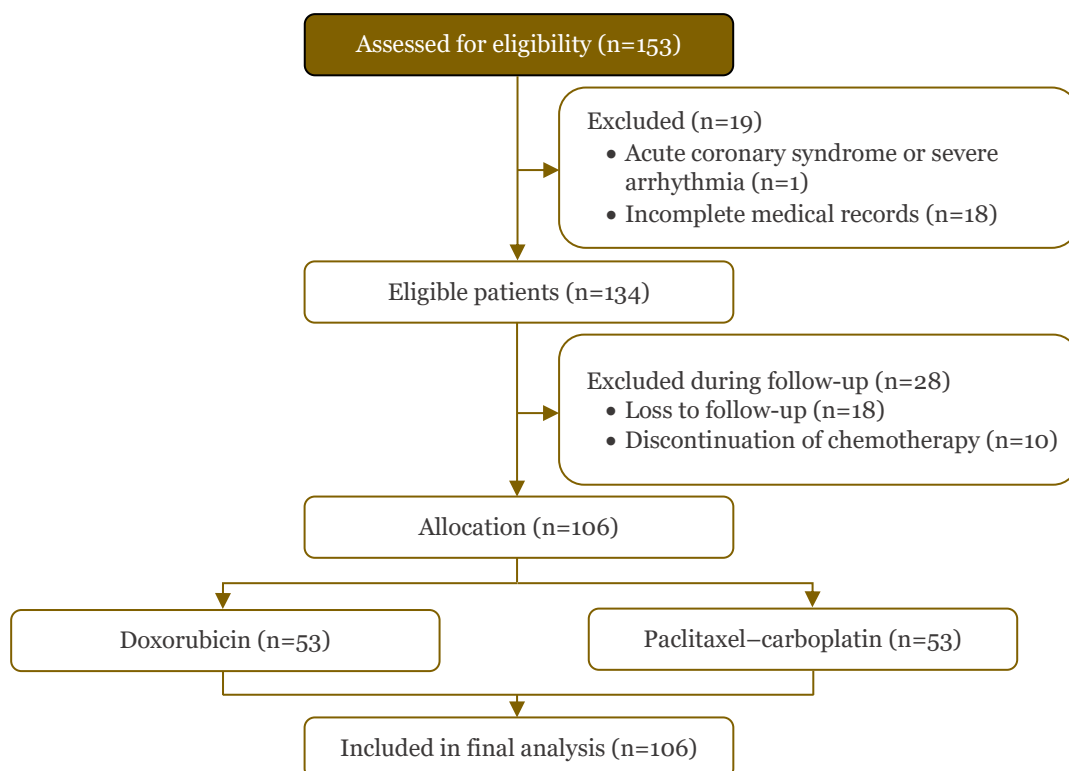


Figure 1. Flow of patient selection and analysis.

Characteristics of patients

Baseline characteristics of patients are presented in **Table 1**. The doxorubicin group was younger than those in the paclitaxel–carboplatin group (48.18 ± 9.47 vs 53.58 ± 8.49 years; $p=0.003$) (**Table 1**). BMI did not differ significantly between groups (19.66 ± 1.33 vs 19.83 ± 1.23 ; $p=0.511$).

All patients had a diagnosis of breast cancer. Comorbidities, including diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, and chronic kidney disease, were comparable between groups (all $p > 0.05$). Similarly, tumor stage (TNM classification) did not differ significantly across groups (all $p > 0.05$). No significant differences were observed in systolic blood pressure (134.35 ± 8.82 vs 135.77 ± 9.68 mmHg; $p = 0.434$) or diastolic blood pressure (81.66 ± 5.53 vs 82.37 ± 5.92 mmHg; $p = 0.521$). However, the cumulative chemotherapy dose was significantly higher in the doxorubicin group compared with the paclitaxel–carboplatin group (507.83 ± 23.42 vs 322.45 ± 48.67 ; $p < 0.001$).

Table 1. Patient characteristics included in this study

Variable	Doxorubicin	Paclitaxel-carboplatin	<i>p</i> -value
	group (n=53)	group (n=53)	
	n (%)	n (%)	
Age (years), mean±SD	48.18±9.47	53.58±8.49	0.003 ^a
Body mass index (kg/m ²), mean±SD	19.66±1.33	19.83±1.23	0.511 ^a
Comorbidities, n (%)			
Diabetes mellitus	26 (49.1)	20 (37.7)	0.240 ^b
Hypertension	38 (71.7)	35 (71.7)	0.529 ^b
Dyslipidemia	46 (89.8)	42 (79.2)	0.301 ^b
Coronary artery disease	0 (0.0)	0 (0.0)	-
Chronic kidney disease	1 (1.9)	1 (1.9)	1.000 ^b
Breast cancer stage (TNM), n (%)			
T2N1Mo	11 (20.8)	7 (13.5)	0.170 ^b
T3NoMo	8 (15.1)	9 (17.3)	0.170 ^b
T3N1Mo	8 (15.1)	7 (13.5)	0.142 ^b
T4bN1Mo	10 (18.9)	11 (21.2)	0.198 ^b
T4bN2Mo	7 (13.2)	8 (15.4)	0.142 ^b
Other stages	9 (17.0)	10 (19.1)	-
Systolic blood pressure (mmHg), mean±SD	134.35±8.82	135.77±9.68	0.434 ^a
Diastolic blood pressure (mmHg), mean±SD	81.66±5.53	82.37±5.92	0.521 ^a
Cumulative chemotherapy dose (mg/m ²), mean±SD	507.83±23.42	322.45±48.67	<0.001 ^a

^a Analyzed using Student's t-test

^b Analyzed using the Chi-squared test

*Statistically significant at $p < 0.05$

Comparison of baseline and four-month left ventricular GLS and LVEF between doxorubicin and paclitaxel–carboplatin chemotherapy groups

Baseline GLS did not differ significantly between the doxorubicin and paclitaxel–carboplatin groups (-20.47 ± 0.45 vs -20.38 ± 0.53 ; $p = 0.410$) (**Table 2**). After four months of chemotherapy, however, GLS differed significantly between groups, with a greater reduction observed in the doxorubicin group compared with the paclitaxel–carboplatin group (-15.04 ± 0.35 vs -19.54 ± 0.50 ; $p < 0.001$). The change in GLS (Δ GLS) was also significantly greater in the doxorubicin group (-5.43 ± 0.12 vs -0.84 ± 0.11 ; $p < 0.001$). In contrast, no significant differences were observed in LVEF either before chemotherapy (55.26 ± 1.78 vs 55.39 ± 1.99 ; $p = 0.720$) or after four months (51.32 ± 1.51 vs 51.60 ± 1.64 ; $p = 0.359$). Similarly, the change in LVEF (Δ LVEF) did not differ significantly between groups (3.93 ± 1.21 vs 3.79 ± 0.98 ; $p = 0.484$) (**Table 2**).

Table 2. Comparison of left ventricular global longitudinal strain (GLS) and left ventricular ejection fraction (LVEF) between doxorubicin and paclitaxel–carboplatin groups

Variable	Doxorubicin	Paclitaxel-carboplatin	<i>p</i> -value ^a
	group (n=53)	group (n=53)	
	Mean±SD	Mean±SD	
GLS before chemotherapy (%)	-20.47±0.45	-20.38±0.53	0.410
GLS 4 months after chemotherapy (%)	-15.04±0.35	-19.54±0.50	<0.001 [*]
Δ GLS (%)	-5.43±0.12	-0.84±0.11	<0.001 [*]
LVEF before chemotherapy (%)	55.26±1.78	55.39±1.99	0.720
LVEF 4 months after chemotherapy (%)	51.32±1.51	51.60±1.64	0.359
Δ LVEF (%)	3.93±1.21	3.79±0.98	0.484

GLS: global longitudinal strain; LVEF: left ventricular ejection fraction

^a Analyzed using the student's t-test

* Statistically significant at $p < 0.05$

A multivariable linear regression analysis showed excellent model fit for GLS ($R=0.984$; $R^2=0.968$), indicating that the variables included in the model explained approximately 96.8% of the variability in GLS (**Table 3**). Among all covariates, only the chemotherapy regimen was significantly associated with GLS. The paclitaxel–carboplatin regimen was associated with significantly lower GLS values compared to doxorubicin ($\beta: -4.902$; SE: 0.234; $t: -20.956$; $p<0.001$), suggesting a more favorable effect on subclinical systolic function than doxorubicin. In contrast, age, systolic and diastolic blood pressure, BMI, and comorbidities, including hypertension, diabetes mellitus, dyslipidemia, and chronic kidney disease, as well as cumulative dose, were not significantly associated with GLS (all $p>0.05$).

Table 3. Multivariable linear regression analysis of factors associated with global longitudinal strain (GLS)

Variable	β	SE	t	p-value ^a
Intercept	-16.133	1.608	-10.030	<0.001*
Age (years)	0.003	0.005	0.637	0.526
Systolic blood pressure (mmHg)	0.018	0.029	0.608	0.545
Diastolic blood pressure (mmHg)	-0.019	0.050	-0.387	0.699
Body mass index (kg/m ²)	0.040	0.034	1.180	0.241
Hypertension (no vs yes)	0.212	0.171	1.240	0.218
Diabetes mellitus (no vs yes)	0.102	0.093	1.097	0.275
Dyslipidemia (no vs yes)	0.053	0.130	0.406	0.686
Chronic kidney disease (no vs yes)	0.108	0.331	0.327	0.744
Chemotherapy regimen (paclitaxel–carboplatin vs doxorubicin)	-4.902	0.234	-20.956	<0.001*
Cumulative dose (mg/m ²)	-0.002	0.001	-1.716	0.089

Model fit $R=0.984$; $R^2=0.968$

^a Analyzed using multivariate linear regression

* Statistically significant at $p<0.05$

Discussion

In this prospective cohort study, patients receiving doxorubicin-based chemotherapy demonstrated a marked decline in GLS after four months, whereas GLS was relatively preserved among those treated with paclitaxel–carboplatin. Baseline myocardial deformation was comparable between groups, with GLS values within the normal range before chemotherapy, supporting the interpretation that the subsequent decline primarily reflected treatment-related myocardial injury rather than pre-existing ventricular dysfunction. In contrast, LVEF remained comparable between groups before and after chemotherapy, indicating that the reduction in GLS represented early subclinical left ventricular systolic impairment that was not captured by conventional LVEF assessment. These findings highlight the greater sensitivity of GLS for detecting early anthracycline-related cardiotoxicity and support its role as a sensitive marker of chemotherapy-related myocardial injury, particularly in patients exposed to anthracycline-based regimens [12].

These findings in this present study are consistent with previous prospective studies showing that GLS can identify early myocardial dysfunction before a detectable decline in LVEF. A previous study reported that a relative reduction in GLS from baseline was a strong predictor of subsequent CTRCD, even among patients with preserved LVEF [12]. Similarly, another study showed that longitudinal strain was more sensitive than radial or circumferential strain for detecting early cardiotoxicity in patients treated with anthracyclines and HER2-targeted therapies [13]. Long-term survivor data further demonstrated persistent GLS impairment despite preserved LVEF, suggesting that myocardial deformation abnormalities may serve as an early and durable marker of anthracycline-related myocardial injury [14].

In the present study, baseline GLS values were comparable between patients receiving doxorubicin and those treated with paclitaxel–carboplatin, indicating similar pre-treatment myocardial function. However, after four months, GLS declined significantly in the doxorubicin group, whereas it remained relatively stable in the paclitaxel–carboplatin group. This divergence is consistent with the established pattern of anthracycline cardiotoxicity, in which impairment of longitudinal myocardial deformation emerges earlier than detectable changes in LVEF [12,13,15].

Furthermore, meta-analyses have reinforced the prognostic value of strain imaging for early detection of chemotherapy-related myocardial dysfunction [16]. Absolute GLS changes of 2–3% or relative reductions of 10–15% have been proposed as clinically meaningful thresholds for identifying subclinical cardiotoxicity [16]. Similarly, patients who developed cardiotoxicity were shown to have greater strain reduction than those without cardiotoxic events, while preserved baseline GLS was associated with a lower risk of subsequent cardiotoxicity [9]. Nevertheless, the clinical impact of GLS-guided surveillance remains under investigation. The SUCCOUR trial did not demonstrate a significant difference in one-year LVEF outcomes between GLS-guided and LVEF-guided monitoring strategies [12]. This finding does not negate the diagnostic sensitivity of GLS, but rather highlights the need for refined thresholds and integrated management strategies so that early strain abnormalities can be translated into improved clinical outcomes.

Although the present study focused on breast cancer patients receiving anthracycline-based chemotherapy, GLS abnormalities have also been documented across other malignancies and treatment modalities. In lymphoma, baseline GLS has been associated with subsequent ventricular dysfunction and heart failure–related hospitalization after anthracycline therapy [17–19]. In pediatric leukemia survivors, a previous study showed that GLS was superior to conventional echocardiography for detecting early cardiotoxicity, which is particularly relevant in long-term survivorship [20]. Beyond anthracyclines, reductions in GLS have been reported in colorectal cancer patients treated with bevacizumab, multiple myeloma patients receiving proteasome inhibitors, and non-small cell lung cancer patients undergoing radiotherapy, where strain decline has been associated with increased mortality risk [21]. These findings suggest that myocardial deformation imaging may capture different mechanisms of treatment-related myocardial injury, including oxidative stress, microvascular dysfunction, and interstitial remodeling [21]. The present findings are consistent with this broader literature, showing a clear divergence in strain trajectories between anthracycline and non-anthracycline chemotherapy exposure.

Differences in cumulative chemotherapy dose should be considered when comparing cardiotoxicity between anthracycline-based chemotherapy and paclitaxel–carboplatin regimens. Doxorubicin has well-established dose-dependent cardiotoxicity, in which higher cumulative exposure is associated with an increased risk of left ventricular dysfunction [22,23]. This effect is mediated by oxidative stress, mitochondrial injury, and activation of apoptotic pathways, leading to progressive myocardial damage [22,24]. GLS is a sensitive parameter for detecting this early injury, as reductions in GLS during anthracycline therapy can predict cardiotoxicity and often precede changes in LVEF. A relative GLS decline of $\geq 15\%$ is commonly used to define subclinical dysfunction [25,26]. In contrast, paclitaxel–carboplatin regimens generally have a milder cardiotoxic profile, with less consistent dose–response effects on myocardial function. In the present study, the greater GLS reduction observed in the doxorubicin group was likely related to higher cumulative anthracycline exposure, underscoring cumulative dose as an important determinant of myocardial impairment and a potential confounder in intergroup comparisons. Frailty may also modify cardiotoxic risk, as reduced physiological reserve, chronic inflammation, and mitochondrial dysfunction can increase susceptibility to myocardial injury [27–29]. However, despite a potentially higher frailty burden in the paclitaxel–carboplatin group, GLS decline remained more pronounced among patients receiving doxorubicin, suggesting that dose-dependent anthracycline toxicity exerted a dominant effect.

The multivariable linear regression model showed excellent explanatory capacity for GLS ($R^2=0.968$), indicating that the included variables collectively explained most of the observed variability in myocardial deformation. Among the covariates entered into the model, including age, systolic blood pressure, body mass index, comorbid conditions, and cumulative chemotherapy dose, only chemotherapy regimen was independently associated with GLS ($\beta=-4.902$; $p<0.001$). This finding indicates that, after adjustment for potential confounders, compared with doxorubicin, paclitaxel–carboplatin was associated with GLS values approximately 4.9 units more negative, indicating better preserved myocardial deformation. The absence of significant associations between GLS and traditional cardiovascular risk factors may reflect the dominant influence of chemotherapy exposure during the early follow-up period, together with the relatively homogeneous baseline characteristics of the study population.

Similarly, the non-significant association between cumulative dose and GLS may be explained by limited variability in administered doses and the short observation window, which may not have been sufficient to capture dose-dependent myocardial injury that typically evolves over a longer duration of exposure.

This study has several limitations that should be acknowledged. The follow-up period was relatively short, as the four-month assessment captured only early cardiotoxicity and did not reflect the long-term trajectory of anthracycline-induced left ventricular dysfunction or its clinical outcomes. Relevant laboratory markers, such as troponin, NT-proBNP, hemoglobin, renal function, and inflammatory markers, were not assessed. Potential confounders, including cardioprotective therapies, cardiovascular risk factors, and comorbidities, may also not have been fully accounted for and could have influenced the observed myocardial response to chemotherapy. Future studies should determine whether early GLS decline predicts long-term ventricular remodeling and clinical heart failure beyond the early post-chemotherapy phase. Large prospective cohorts are needed to refine clinically actionable strain thresholds and improve standardization across imaging techniques. Future studies should also incorporate diagnostic performance analyses to establish the sensitivity and specificity of GLS, thereby better defining its utility as an early marker of chemotherapy-induced cardiotoxicity in breast cancer patients. Integration of deformation imaging with biomarkers and advanced tissue characterization could further enhance risk stratification and deepen understanding of the biological mechanisms underlying chemotherapy-related myocardial injury.

Conclusion

Doxorubicin-based chemotherapy was associated with a significant early decline in left ventricular GLS, despite preserved baseline myocardial function, whereas paclitaxel–carboplatin regimens demonstrated relative stability in myocardial deformation, supporting the sensitivity of GLS in detecting subclinical anthracycline-related myocardial dysfunction before overt reduction in LVEF becomes apparent. Incorporation of strain imaging into routine cardio-oncology surveillance may enhance early identification of patients at risk and provide an opportunity for timely preventive intervention.

Ethics approval

The protocol of the present study was reviewed and approved by the Health Research Ethics Committee of Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia (Approval number: 288/ETIK-RSUDZA/2025).

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Competing interests

All authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

An artificial intelligence (AI) tool, ChatGPT, was employed in the language refinement (improving grammar, sentence structure, and readability of the manuscript). We confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

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References

- Harris TJR, McCormick F. The molecular pathology of cancer. *Nat Rev Clin Oncol* 2010;7(5):251–265.
- Bray F, Laversanne M, Sung H, *et al.* Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024;74(3):229–263.
- Arnold M, Morgan E, Runggay H, *et al.* Current and future burden of breast cancer: Global statistics for 2020 and 2040. *Breast* 2022;66:15–23.
- Benitez Fuentes JD, Morgan E, de Luna Aguilar A, *et al.* Global stage distribution of breast cancer at diagnosis. *JAMA Oncol* 2024;10(1):71.
- Christowitz C, Davis T, Isaacs A, *et al.* Mechanisms of doxorubicin-induced drug resistance and drug resistant tumour growth in a murine breast tumour model. *BMC Cancer* 2019;19(1):757.
- Lobefaro R, Mariani L, Peverelli G, *et al.* Efficacy and safety of first-line carboplatin-paclitaxel and carboplatin-gemcitabine in patients with advanced triple-negative breast cancer: A monocentric, retrospective comparison. *Clin Breast Cancer* 2023;23(3):e151–e162.
- Lyon AR, López-Fernández 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). *Eur Heart J* 2022;43(41):4229–4361.
- Sławiński G, Hawryszko M, Liżewska-Springer A, *et al.* Global longitudinal strain in cardio-oncology: A review. *Cancers* 2023;15(3):986.
- Cocco LD, Chiaparin AF, Saffi MAL, *et al.* Global longitudinal strain for the early detection of chemotherapy-induced cardiotoxicity: A systematic review and meta-analysis. *Clin Oncol* 2022;34(8):514–525.
- Plana JC, Galderisi M, Barac A, *et al.* Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: A report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2014;27(9):911–939.
- Brady B, Murphy R. Cancer treatment-related cardiac dysfunction. *BMJ Support Palliat Care* 2023;13(1):53–56.
- Negishi T, Thavendiranathan P, Penicka M, *et al.* Cardioprotection using strain-guided management of potentially cardiotoxic cancer therapy. *JACC Cardiovasc Imaging* 2023;16(3):269–278.
- Sawaya H, Sebag IA, Plana JC, *et al.* Assessment of echocardiography and biomarkers for the extended prediction of cardiotoxicity in patients treated with anthracyclines, taxanes, and trastuzumab. *Circ Cardiovasc Imaging* 2012;5(5):596–603.
- Lipshultz SE, Rifai N, Dalton VM, *et al.* The effect of dexrazoxane on myocardial injury in doxorubicin-treated children with acute lymphoblastic leukemia. *N Engl J Med* 2004;351(2):145–153.
- Sawaya H, Sebag IA, Plana JC, *et al.* Early detection and prediction of cardiotoxicity in chemotherapy-treated patients. *Am J Cardiol* 2011;107(9):1375–1380.
- Oikonomou EK, Kokkinidis DG, Kampaktis PN, *et al.* Assessment of prognostic value of left ventricular global longitudinal strain for early prediction of chemotherapy-induced cardiotoxicity. *JAMA Cardiol* 2019;4(10):1007.
- Demissei BG, Hubbard RA, Zhang L, *et al.* Changes in cardiovascular biomarkers with breast cancer therapy and associations with cardiac dysfunction. *J Am Heart Assoc* 2020;9(2):e014708.
- Esmailzadeh M, Urzua Fresno CM, Somerset E, *et al.* A combined echocardiography approach for the diagnosis of cancer therapy-related cardiac dysfunction in women with early-stage breast cancer. *JAMA Cardiol* 2022;7(3):330.

19. 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.
20. Gonzalez-Manzanares R, Castillo J, Molina J, *et al.* Automated global longitudinal strain assessment in long-term survivors of childhood acute lymphoblastic leukemia. *Cancers* 2022;14(6):1513.
21. Sonaglioni A, Albini A, Fossile E, *et al.* Speckle-tracking echocardiography for cardioncological evaluation in bevacizumab-treated colorectal cancer patients. *Cardiovasc Toxicol* 2020;20(6):581-592.
22. Linders AN, Dias IB, López Fernández T, *et al.* A review of the pathophysiological mechanisms of doxorubicin-induced cardiotoxicity and aging. *NPJ Aging* 2024;10(1):9.
23. Rawat PS, Jaiswal A, Khurana A, *et al.* Doxorubicin-induced cardiotoxicity: An update on the molecular mechanism and novel therapeutic strategies for effective management. *Biomed Pharmacother* 2021;139:111708.
24. Jones RL, Wagner AJ, Kawai A, *et al.* Prospective evaluation of doxorubicin cardiotoxicity in patients with advanced soft-tissue sarcoma treated in the ANNOUNCE phase III randomized trial. *Clin Cancer Res* 2021;27(14):3861-3866.
25. Ruane L, Narendren A, Prasad S, *et al.* Clinical utility of global longitudinal strain in cancer therapy monitoring. *Heart Lung Circ* 2024;33:S297.
26. Araujo-Gutierrez R, Chitturi KR, Xu J, *et al.* Baseline global longitudinal strain predictive of anthracycline-induced cardiotoxicity. *Cardiooncology* 2021;7(1):4.
27. Wang T, Jiang J, Song Z, *et al.* Prevalence of frailty and its predictors among patients with cancer at the chemotherapy stage: Systematic review. *JMIR Cancer* 2025;11:e69936-e69936.
28. Yang S, Lou X, Ahmed MM, *et al.* Impact of pre-existing frailty on cardiotoxicity among breast cancer patients receiving adjuvant therapy. *JACC CardioOncol* 2025;7(2):110-121.
29. Ho YW, Tang WR, Chen SY, *et al.* Association of frailty and chemotherapy-related adverse outcomes in geriatric patients with cancer: A pilot observational study in Taiwan. *Aging* 2021;13(21):24192-24204.