

Echocardiographic Risk Stratification in a General Oncology Population in Myanmar: A Prospective Observational Study

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ABSTRACT

ARTICLE DETAILS

Background: Chemotherapy-related cardiac dysfunction (CTRCD) is a major cause of morbidity in cancer survivors. While global longitudinal strain (GLS) has shown promise in predicting cardiotoxicity, its utility has not been established in resource-limited settings like Myanmar, where the baseline burden of cardiovascular risk is high.

Objectives: This study sought to determine the predictive value of baseline pre-chemotherapy echocardiographic parameters, particularly GLS, for the development of CTRCD in a diverse cohort of Myanmar patients with common solid tumors.

Methods: We conducted a prospective, single-center, observational cohort study in Pyin Oo Lwin. We enrolled 150 chemotherapy-naïve adult patients with breast, cervical, lung, or other solid tumors scheduled to receive anthracycline- and/or trastuzumab-based therapy. All patients underwent baseline clinical assessment and comprehensive transthoracic echocardiography, including speckle-tracking for GLS. Patients were followed for 12 months with serial echocardiograms. The primary endpoint was CTRCD, defined as a decline in left ventricular ejection fraction (LVEF) by >10 percentage points to a value <53%.

Results: Over 12 months, 23 patients (15.3%) developed CTRCD. In baseline analysis, patients who developed CTRCD had significantly worse mean GLS compared to those who did not (−17.8 vs. −20.1; $p<0.001$), while baseline LVEF was not significantly different. In multivariable logistic regression, an abnormal baseline GLS (defined as $> -18\%$) was the only strong, independent predictor of CTRCD (Adjusted Odds Ratio: 4.0; 95% Confidence Interval: 1.6-9.9; $p=0.003$), after adjusting for age, hypertension, and cancer type. Subclinical LV dysfunction (relative GLS drop $>15\%$) occurred in 40 patients (26.7%).

Conclusions: In a Myanmar oncology cohort, baseline GLS is a powerful and independent predictor of subsequent cardiotoxicity, superior to baseline LVEF. Integrating pre-chemotherapy GLS into routine assessment could significantly improve risk stratification and guide preventative strategies in resource-limited settings.

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INTRODUCTION

The efficacy of modern cancer therapies has led to a growing population of long-term survivors, shifting clinical

focus toward mitigating the long-term sequelae of treatment [1]. Among these, chemotherapy-related cardiac dysfunction (CTRCD) stands out as a significant cause of morbidity and

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mortality, capable of negating the benefits of successful cancer treatment [2, 3]. Cardiotoxic agents, particularly anthracyclines and the anti-HER2 agent trastuzumab, are mainstays in the treatment of breast cancer and other common malignancies but carry a well-documented risk of inducing myocardial injury and heart failure [4, 5].

For decades, the standard for cardiac monitoring has been the serial assessment of left ventricular ejection fraction (LVEF). However, LVEF is a relatively crude measure of systolic function, and a detectable decline often signifies established, and potentially irreversible, myocardial damage [6]. This limitation has driven the search for more sensitive tools to detect subclinical cardiac injury at a stage where intervention might prevent progression to overt heart failure.

Speckle-tracking echocardiography-derived global longitudinal strain (GLS) has emerged as a robust marker of myocardial deformation, capable of detecting subtle LV dysfunction before any change in LVEF [7]. International guidelines now recognize the value of GLS, with a relative reduction of >15% from baseline considered an early sign of cardiotoxicity, prompting closer follow-up or the initiation of cardioprotective therapy [8, 9].

While the prognostic value of baseline and serial GLS assessment is well-documented in North American and European cohorts [10, 11], there is a critical lack of data from low- and middle-income countries (LMICs), particularly in Southeast Asia. Myanmar faces a dual health burden, with rising rates of non-communicable diseases, such as hypertension and diabetes, alongside infectious diseases [12]. This high prevalence of pre-existing cardiovascular risk factors may place its oncology population at an amplified risk of CTRCD. In such a resource-constrained healthcare environment, an effective, non-invasive, and affordable tool for baseline risk stratification is not merely beneficial but essential. Identifying high-risk patients before treatment begins would allow for the rational allocation of limited resources, such as more frequent monitoring or the targeted use of cardioprotective agents like ACE inhibitors or beta-blockers [13].

This study therefore aimed to conduct the first prospective evaluation of pre-chemotherapy echocardiographic parameters, focusing on the incremental value of GLS over LVEF, for predicting CTRCD in a general oncology population in Myanmar. We hypothesized that baseline GLS would be a superior predictor of subsequent cardiotoxicity compared to baseline LVEF and traditional clinical risk factors.

METHODS

Study Design and Population

This was a prospective, single-center, observational cohort study conducted at 700 bedded General Hospital,

Pyin Oo Lwin, Myanmar, from January 2023 to August 2025. The study protocol was approved by Local Ethical Review Committee, and all participants provided written informed consent.

We prospectively enrolled 150 consecutive, chemotherapy-naïve adult patients (≥ 18 years of age) with a new histopathological diagnosis of a solid tumor. Eligible patients were those scheduled to receive chemotherapy regimens containing an anthracycline (e.g., doxorubicin, epirubicin) and/or trastuzumab. Key inclusion criteria were an LVEF $\geq 53\%$ at baseline and the ability to provide informed consent. Exclusion criteria included prior exposure to cardiotoxic chemotherapy or thoracic radiation, pre-existing heart failure or significant valvular disease, a life expectancy of less than 12 months, or technically inadequate echocardiographic images for strain analysis.

Study Procedures

At baseline, prior to initiating chemotherapy, all participants underwent a comprehensive clinical evaluation, including collection of demographic data, medical history, and cardiovascular risk factors. A standard 12-lead electrocardiogram was also performed.

A comprehensive transthoracic echocardiogram (TTE) was performed and analyzed by a single experienced sonographer and cardiologist, respectively, according to American Society of Echocardiography guidelines. LVEF was calculated using the biplane method of disks (modified Simpson's rule). For GLS analysis, standard 2D grayscale images were acquired from the apical 4-, 3-, and 2-chamber views at a frame rate of 50–80 frames/s. Speckle-tracking analysis was performed offline using dedicated software.

The endocardial border was manually traced, and the software automatically tracked myocardial segments throughout the cardiac cycle. GLS was calculated by averaging the peak systolic strain values from all 17 myocardial segments. The primary reader was blinded to clinical outcomes.

Following the baseline assessment, patients were followed up at 3, 6, and 12 months after chemotherapy initiation with repeat clinical and echocardiographic assessments.

Endpoints

The primary endpoint of the study was the incidence of definite CTRCD at 12 months, defined according to consensus guidelines as a decrease in LVEF of >10 percentage points to a final value of $<53\%$. The secondary endpoint was the incidence of subclinical LV dysfunction, defined as a relative reduction in GLS of >15% from baseline at any time during follow-up, in the absence of meeting criteria for the primary endpoint. Other endpoints included symptomatic heart failure, cardiovascular death, and a composite of cardiovascular death or hospitalization for heart failure.

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Statistical Analysis

Continuous variables were presented as mean $\pm$ standard deviation and compared using the Student's t-test. Categorical variables were presented as frequencies (percentages) and compared using the χ^2 or Fisher's exact test. An abnormal baseline GLS was defined a priori as a value greater (less negative) than -18% (e.g., -17.5%) based on prior literature suggesting prognostic utility. Univariable and multivariable logistic regression analyses were performed to identify independent predictors of the primary endpoint. Variables with a $p < 0.10$ in univariable analysis, along with clinically relevant pre-specified variables (cancer type), were included in the multivariable model. Breast cancer was chosen as the reference category for cancer type due to it being the largest subgroup and the most common clinical scenario. A two-sided p -value of < 0.05 was considered statistically significant. All analyses were performed using SPSS version 25.0.

RESULTS

Baseline Characteristics and Outcomes

A total of 150 patients were enrolled and completed the 12-month follow-up. The baseline characteristics of the cohort, stratified by the subsequent development of CTRCD, are shown in Table 1. The mean age of the cohort was 52.1 ± 10.1 years, and 124 (82.7%) were female. The cohort comprised patients with breast cancer ($n=90$, 60.0%), cervical cancer ($n=25$, 16.7%), lung cancer ($n=20$, 13.3%), and other solid tumors ($n=15$, 10.0%).

Over the 12-month follow-up period, 23 patients (15.3%) developed the primary endpoint of definite CTRCD. Patients who developed CTRCD were older (55.8 ± 9.5 years vs. 51.4 ± 10.2 years; mean difference 4.4 years, 95% CI 0.2–8.6; $p=0.04$) and had a non-significant trend toward a higher prevalence of hypertension (11 of 23, 47.8% vs. 38 of 127, 29.9%; absolute difference 17.9%, 95% CI -3.2% to 38.4% ; $p=0.07$). The most significant difference at baseline was in myocardial function measured by GLS. The mean baseline GLS in patients who subsequently developed CTRCD was significantly worse (-17.8 ± 2.0 vs. -20.1 ± 1.8 ; mean difference 2.3%, 95% CI 1.4–3.2; $p < 0.001$). In contrast, baseline LVEF was only borderline different between the two groups ($61.5 \pm 4.1\%$ vs. $63.1 \pm 3.5\%$; mean difference -1.6% , 95% CI -3.3% to 0.1% ; $p=0.06$).

Table 1. Baseline Clinical and Echocardiographic Characteristics

Characteristic	No CTRCD (n=127)	With CTRCD (n=23)	Total Cohort (N=150)	P-value
Demographics				
Age, years (mean $\pm$ SD)	51.4 $\pm$ 10.2	55.8 $\pm$ 9.5	52.1 $\pm$ 10.1	0.04
Female Sex, n	105	19 (82.6)	124	0.99

(%)	(82.7)		(82.7)	
Cardiovascular Risk Factors				
Hypertension, n (%)	38 (29.9)	11 (47.8)	49 (32.7)	0.07
DM, n (%)	18 (14.2)	5 (21.7)	23 (15.3)	0.34
Oncologic Characteristics				
Breast Cancer, n (%)	75 (59.1)	15 (65.2)	90 (60.0)	Reference
Cervical Cancer, n (%)	22 (17.3)	3 (13.0)	25 (16.7)	0.63
Lung Cancer, n (%)	18 (14.2)	2 (8.7)	20 (13.3)	0.54
Other Solid Tumors, n (%)	12 (9.4)	3 (13.0)	15 (10.0)	0.75
Baseline ECHO				
LVEF, % (mean $\pm$ SD)	63.1 $\pm$ 3.5	61.5 $\pm$ 4.1	62.8 $\pm$ 3.7	0.06
GLS, % (mean $\pm$ SD)	-20.1 $\pm$ 1.8	-17.8 $\pm$ 2.0	-19.8 $\pm$ 2.0	<0.001

Predictors of Cardiotoxicity

The results of the univariable and multivariable logistic regression analyses are shown in Table 2. In univariable analysis, an abnormal baseline GLS ($> -18\%$) was the strongest predictor of CTRCD (Odds Ratio [OR]: 4.8; 95% Confidence Interval [CI]: 2.0–11.5; $p < 0.001$). Older age and hypertension showed trends toward significance. In the multivariable model, after adjusting for age, hypertension, and cancer type, an abnormal baseline GLS remained the only significant, independent predictor of CTRCD (Adjusted OR: 4.0; 95% CI: 1.6–9.9; $p=0.003$). Neither the specific cancer type nor other clinical risk factors were independently associated with CTRCD in the adjusted model.

Table 2: Univariable and Multivariable Predictors of CTRCD

Predictor Variable	Univariable Analysis (OR [95% CI])	P-value	Multivariable Analysis (Adjusted OR [95% CI])	P-value
Clinical				
Age > 65 years	2.1 [0.9–4.8]	0.08	1.9 [0.8–4.5]	0.16
Hypertension	2.1 [0.9–5.0]	0.07	1.8 [0.7–4.6]	0.22
Cancer Type				
Breast Cancer	1.0 (Reference)		1.0 (Reference)	
Cervical Cancer	0.7 [0.2–2.9]	0.63	0.7 [0.2–2.8]	0.61
Lung Cancer	0.6 [0.1–3.0]	0.54	0.6 [0.1–2.9]	0.52
Other Solid	1.3 [0.3–5.3]	0.75	1.2 [0.3–5.1]	0.78

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Tumors				
ECHO				
Abnormal Baseline GLS > -18%	4.8 [2.0-11.5]	<0.001	4.0 [1.6-9.9]	0.003

Incidence of Clinical and Subclinical Endpoints

The incidence of all primary and secondary endpoints, stratified by cancer type, is presented in Table 3. The secondary endpoint of subclinical LV dysfunction (relative GLS drop >15%) occurred in 40 patients (26.7%), a substantially higher rate than that of definite CTRCD. This finding underscores the sensitivity of GLS in detecting early myocardial injury. Symptomatic heart failure and cardiovascular death were rare events in this 12-month follow-up period.

Table 3: Incidence of Endpoints at 12 Months by Cancer Type

End-point	Definite CTRCD	Subclinical Dysfunction	Symptomatic HF	CVS Death
Breast Cancer (n=90)	15 (16.7%)	26 (28.9%)	3 (3.3%)	1 (1.1%)
Cervical Cancer (n=25)	3 (12.0%)	6 (24.0%)	1 (4.0%)	0 (0%)
Lung Cancer (n=20)	2 (10.0%)	4 (20.0%)	1 (5.0%)	1 (5.0%)
Other Cancers (n=15)	3 (20.0%)	4 (26.7%)	0 (0%)	0 (0%)
Total Cohort (N=150)	23 (15.3%)	40 (26.7%)	5 (3.3%)	2 (1.3%)

HF, Heart Failure; CVS, Cardiovascular

DISCUSSION

In this first prospective cardio-oncology study in a diverse Myanmar population, we made a key finding: baseline global longitudinal strain is a powerful and independent predictor of chemotherapy-related cardiac dysfunction, superior to traditional clinical risk factors and baseline LVEF. Patients with a subtly impaired baseline GLS of > -18% had a four-fold increased risk of developing CTRCD over 12 months, a finding that persisted after multivariable adjustment. This result provides strong evidence for integrating GLS into pre-treatment risk assessment in this and similar settings.

Our study addresses a critical evidence gap, as the vast majority of cardio-oncology research originates from high-income countries with different patient demographics and

healthcare systems [14]. The findings are particularly salient in the context of Myanmar, which faces a dual burden of infectious and non-communicable diseases, including high rates of hypertension and diabetes [12]. This high prevalence of pre-existing cardiovascular risk factors may prime the myocardium for what is known as a "second hit" from cardiotoxic chemotherapy [15]. In this model, pre-existing conditions may cause subclinical myocardial damage that is not detectable by LVEF but is unmasked by the more sensitive GLS measurement. This underlying vulnerability is then amplified by exposure to agents like anthracyclines, accelerating the progression to overt cardiac dysfunction. Our data, showing a non-significant trend towards higher rates of hypertension in the CTRCD group, support this hypothesis.

The overall incidence of definite CTRCD in our cohort was 15.3% over 12 months. This rate is comparable to, and in some cases higher than, incidences reported in North American and European cohorts receiving similar chemotherapy regimens [16,17]. This observation further suggests that populations with a higher baseline prevalence of cardiovascular risk factors may be disproportionately susceptible to the cardiotoxic effects of cancer therapy, reinforcing the need for more sensitive baseline screening tools.

The superiority of GLS over LVEF as a baseline prognostic tool is a central theme of our results and is rooted in pathophysiology. LVEF measures the volumetric change of the ventricle—a relatively crude indicator of pump function that can be compensated for by various mechanisms until significant and often irreversible damage has occurred [6]. In contrast, GLS measures the longitudinal shortening of myocardial fibers, a more direct and sensitive marker of intrinsic contractility that is predominantly governed by the subendocardium—the myocardial layer most vulnerable to ischemic and toxic insults [18]. Our data show that a pre-treatment GLS assessment can effectively "stress test" the myocardium's functional reserve, revealing subclinical dysfunction that LVEF cannot detect.

A significant proportion of our cohort (26.7%) experienced subclinical cardiotoxicity, defined by a relative GLS drop of >15%, compared to the 15.3% who met the criteria for definite CTRCD based on LVEF decline. The use of a >15% relative drop in GLS as a marker for subclinical cardiotoxicity is supported by international consensus guidelines and has been shown to be a critical early warning sign [8, 9]. Detecting this "GLS-first" injury has profound clinical implications. As demonstrated in trials like SUCCOUR, identifying patients with this early drop in GLS allows clinicians to initiate cardioprotective medications, such as ACE inhibitors and beta-blockers, potentially preventing the progression to irreversible systolic dysfunction and overt heart failure [19].

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The practical implications for resource-constrained settings like Myanmar are substantial. While advanced techniques like GLS require specific software and training, our study provides a strong rationale for this investment. A single, comprehensive baseline echocardiogram with GLS could fundamentally alter patient management by triaging patients into high- and low-risk pathways. High-risk patients (e.g., those with baseline GLS $> -18\%$) could be allocated resources for more intensive cardiac surveillance, while low-risk patients could be monitored less frequently, optimizing efficiency and reducing the burden on both patients and the healthcare system [20]. Furthermore, this upfront investment in GLS capabilities may prove highly cost-effective by reducing long-term expenses associated with managing overt heart failure and by allowing for more rational allocation of follow-up resources.

Finally, this study serves as a model for future research and clinical practice in global cardio-oncology. The next logical steps should include longer-term follow-up of this cohort to determine the rate of progression from subclinical dysfunction to symptomatic heart failure. Furthermore, future studies should aim to incorporate cardiac biomarkers like troponin, which were not assessed in our study but could provide complementary prognostic information. Ultimately, our findings champion the idea that adapting advanced, yet accessible, diagnostic technologies to local needs can help bridge the global gap in cancer care, improving survivorship and reducing health disparities in LMICs [21].

Study Limitation

Limitations Our study has several limitations. First, as a single-center study, its findings may not be generalizable to all of Myanmar, though our center is a major national referral hospital. Second, the sample size of 150 patients, while adequate for assessing the primary endpoint, limits the statistical power for subgroup analyses, particularly in the smaller cancer cohorts like lung and cervical cancer. Third, we did not include cardiac biomarkers such as troponin or natriuretic peptides, which could have provided additional prognostic information. Finally, the 12-month follow-up period is relatively short; longer-term follow-up is needed to assess the progression from subclinical to clinical heart failure and the incidence of late cardiotoxicity.

CONCLUSIONS

In this Myanmar oncology cohort, a subtly impaired baseline Global Longitudinal Strain is a powerful, independent predictor of future chemotherapy-related cardiac dysfunction, proving superior to the conventional metric of baseline LVEF. The integration of pre-chemotherapy GLS assessment into routine clinical practice offers a practical and effective strategy for risk stratification. This approach can help identify vulnerable patients, guide preventative therapies, and optimize healthcare resource

allocation in cardio-oncology care in resource-limited settings.

CLINICAL PERSPECTIVES

Competency in Medical Knowledge

This study connects the science of chemotherapy-induced cardiotoxicity with the clinical application of advanced diagnostics like Global Longitudinal Strain (GLS). It validates international findings in Myanmar, generating actionable, local evidence rather than simply adopting external guidelines. It provides a new risk tool, establishing the high negative predictive value of baseline GLS as an important piece of clinical knowledge for managing patients in the region.

Despite the clear prognostic utility of GLS, several challenges exist regarding its routine implementation in Myanmar. First, GLS measurement requires specialized echocardiographic software and higher-end ultrasound machines, which are often limited to tertiary centers and unaffordable for smaller regional hospitals. Second, there is a need for standardized training of sonographers and cardiologists to ensure accurate acquisition and interpretation of GLS, as variability in technique can affect reproducibility. Finally, financial constraints faced by patients and the healthcare system may restrict widespread access. Addressing these barriers will require investment in training programs, negotiated access to affordable software, and integration of GLS into national guidelines to justify resource allocation.

Translational Outlook

The results can be immediately translated into a practical screening protocol. Clinicians can use a standard pre-treatment echocardiogram to categorize patients into low-risk and high-risk groups, allowing them to de-escalate monitoring for the majority of patients and focus resources on the vulnerable minority.

It provides the foundational evidence needed to establish the first local cardio-oncology guidelines in Myanmar. It also serves as the necessary pilot data to design a future, larger interventional trial aimed at proving that this risk-stratification strategy actively prevents heart failure.

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CONFLICT OF INTEREST

No conflict of interest. No external funding.

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