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Original Research Article

Assessment of the Prognostic Value of Left Ventricular Global Longitudinal Strain for Early Prediction of Cardiotoxicity Among Adult Cancer Patients Receiving Cardiotoxic Chemotherapy

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Abstract:

Introduction: The evaluation of global longitudinal strain (GLS) is recognised in cardio-oncology for the early detection of cardiotoxicity associated with anticancer therapies. Baseline left ventricular (LV) global longitudinal strain (GLS) and right ventricular (RV) GLS evaluations can detect patients predisposed to systolic dysfunction and heart failure resulting from the cardiotoxic effects of many cancer therapies. Progress in the early identification and management of cancer has markedly decreased mortality rates. The outcome is the formation of a group of patients whose survival is adequate to demonstrate the side effects of the administered medicines. Cardiotoxicity refers to the array of cardiovascular disorders induced by onco-hematological therapies.

Objectives: To assess the significance of global longitudinal strain in the early identification of cardiotoxicity in individuals receiving chemotherapy.

Method: A quantitative, analytical, prospective, longitudinal study was carried out in 100 patients diagnosed with breast cancer or lymphoma, who started chemotherapy treatment at Department of Cardiology, S.C.B. Medical College and Hospital, Cuttack, Odisha. Primary and secondary methods were used for raw data collection and several statistical tests were used for its analysis.

Results: The notable association between GLS and chemotherapy dosage underscores the necessity of monitoring cumulative exposure and the potential for early intervention with cardioprotective therapies. this investigation demonstrated a modest positive connection between GLS and LVEF ($r = 0.61$, $p < 0.001$), reinforcing the notion that these two echocardiographic parameters are interconnected, but not synonymous. A moderate negative correlation ($r = -0.52$, $p < 0.001$) identified in our investigation between cumulative chemotherapeutic dosage and global longitudinal strain (GLS) underscores a distinct dose-dependent association between cardiotoxic exposure and myocardial strain deterioration. The fall in GLS occurs prior to the loss in LVEF, establishing it as a more effective early diagnostic instrument for cardiotoxicity.

Conclusions: Global longitudinal strain is an echocardiographic measure of cardiac function that demonstrates strong discriminatory value regarding cardiotoxicity in patients undergoing chemotherapy.

Keywords: Chemotherapy-induced cardiotoxicity, Global longitudinal strain, Chemotherapy, echocardiography, left ventricular, right ventricular.

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Introduction

Cancer patients now experience significantly improved survival rates due to advancements in cancer therapies; however, the incidence of cancer therapy-related cardiac dysfunction (CTRCD) is increasing as a result of the heightened utilisation of cardiotoxic chemotherapeutic agents such as trastuzumab, anthracyclines, and immune checkpoint inhibitors [1]. Effective cancer treatment is significantly obstructed by cardiotoxicity, often resulting in treatment cessation, diminished quality of life, and heightened cardiovascular morbidity and mortality [2]. Consequently, timely cardioprotective interventions and favourable oncologic results rely on the early identification of subclinical dysfunction.

The primary method for monitoring cardiac function during chemotherapy has traditionally been the standard echocardiographic assessment of left

ventricular ejection fraction (LVEF). Nonetheless, LVEF typically does not decline until significant and often irreversible damage has occurred, and it lacks sensitivity to early myocardial injury [2]. This limitation underscores the necessity for novel sensitive imaging biomarkers capable of detecting myocardial dysfunction prior to the onset of the overt heart failure.

Two-dimensional speckle-tracking echocardiography-derived left ventricular global longitudinal strain (LV GLS) has emerged as a promising technique for the early identification of myocardial injury. Longitudinal myocardial fibre distortion, which is more vulnerable to cardiotoxic injury, is indicated by GLS [4]. Numerous studies indicate that a relative decline in GLS signifies impending CTRCD and precedes changes in LVEF. In patients with preserved LVEF, a clinically meaningful indicator of early cardiotoxicity is proposed to be a relative decrease of ≥15% from baseline GLS [5].

The predictive efficacy of GLS in forecasting early cardiotoxicity in diverse adult cancer populations undergoing cardiotoxic chemotherapy requires further confirmation, particularly in real-world clinical environments, despite increasing evidence endorsing its clinical significance. GLS-based risk stratification may be influenced by variations in cardiovascular risk profiles, cancer kinds, treatment regimens, and follow-up durations [6].

Objectives

The main aim of this study is to evaluate the prognostic significance of left ventricular global longitudinal strain in the early detection of cardiotoxicity in adult cancer patients undergoing cardiotoxic chemotherapy.

Methodology

Study Design: This study was a prospective observational study.

Study Setting: The study was carried out at the Department of Cardiology, S.C.B. Medical College and Hospital, Cuttack, Odisha.

Study Duration: The study was conducted over a period of 18 months.

Participants: A total of 100 cancer patients were enrolled for this study. Eligible patients were recruited from the Cardiology OPD before the initiation of chemotherapy. The following baseline data were recorded:

Demographics: Age, sex.

- Clinical details: Comorbidities (hypertension, diabetes), type and stage of cancer
- Chemotherapy regimen: Agents used, cumulative dose, number of cycles
- Baseline labs: ECG, CBC, RFT, LFT, serum electrolytes, and cardiac biomarkers (Troponin I, NT-proBNP)

Inclusion Criteria

- Age ≥18 years
- Diagnosed with any type of malignancy
- Eligible to receive cardiotoxic chemotherapy (e.g., anthracyclines, trastuzumab)
- Referred for baseline cardiology evaluation before chemotherapy
- Willing to provide informed written consent

Exclusion Criteria

- Baseline LVEF < 50%
- Baseline GLS < -16%
- Known congenital or significant valvular heart disease
- History of myocardial infarction, cardiac surgery, or coronary intervention
- Diagnosed cardiomyopathy
- Use of ACE inhibitors or beta-blockers prior to chemotherapy

Echocardiographic Evaluation: Echocardiographic assessments were performed using the GE Vivid T8 machine by a trained cardiologist at three time points:

1. Baseline (pre-chemotherapy)
2. 3 months post-chemotherapy initiation
3. 6 months post-chemotherapy initiation

Statistical Analysis: Data were analyzed using SPSS v26.0 and GraphPad Prism v10. A p value < 0.05 were considered statistically significant.

Results

1. **Demographic and Clinical Characteristics**

Parameter	**Value (n = 100)**
Mean Age (years)	52.4 ± 11.8
Gender (Female: Male)	70: 30
Type of Malignancy	
Breast Cancer	60 (60%)
Lung Cancer	20 (20%)
Lymphoma	12 (12%)
Other Malignancies	8 (8%)
Comorbidities	

Hypertension	38 (38%)
Diabetes Mellitus	31 (31%)
Mean Baseline LVEF (%)	61.7 ± 4.3
Mean Baseline GLS (%)	-19.5 ± 1.1

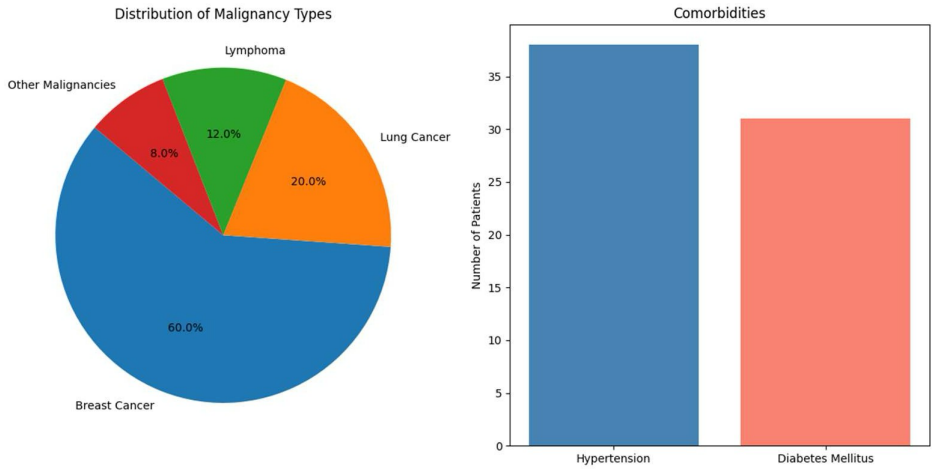

Figure 1: Baseline characteristics of the study population (n=100)

A. Pie chart showing the distribution of malignancy types, with breast cancer as the predominant diagnosis (60%), followed by lung cancer (20%), lymphoma (12%), and other malignancies (8%).

B. Bar graph illustrating the prevalence of comorbid conditions, with hypertension (38%) and diabetes mellitus (31%) being the most common.

2. **Incidence of Left Ventricular Dysfunction**

LVD Type	**n (%)**
Subclinical LVD (GLS > -18%, LVEF ≥ 50%)	20 (20%)
Overt LVD (LVEF < 50%)	6 (6%)
No LVD	74 (74%)

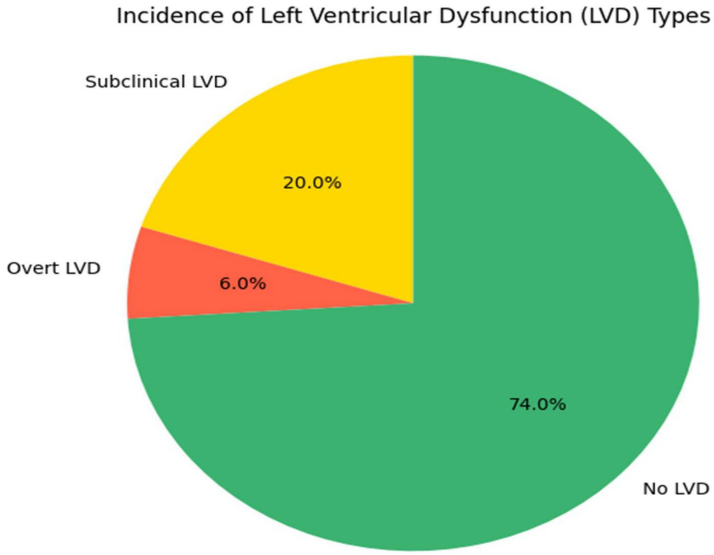

Figure 2: Distribution of Left Ventricular Dysfunction (LVD) types among chemotherapy-treated cancer patients (n = 100). The pie chart illustrates the proportion of patients who developed subclinical LVD (20%), overt LVD (6%), and those who did not exhibit any LVD (74%) over a 6-month follow- up period.

3. **GLS and LVEF Changes Over Time**

a) Global Longitudinal Strain (GLS) Changes

Time Point	Mean GLS (%) ± SD
Baseline	-19.5 ± 1.1
3 Months Post-Chemo	-18.2 ± 1.5
6 Months Post-Chemo	-17.3 ± 1.8

b) Left Ventricular Ejection Fraction (LVEF) Changes

Time Point	Mean LVEF (%) ± SD
Baseline	61.7 ± 4.3
3 Months Post-Chemo	58.9 ± 5.1
6 Months Post-Chemo	56.8 ± 6.5

4. **GLS as a Predictor of Subclinical LVD**

- ROC Curve Analysis:
  - AUC = 0.91 (95% CI: 0.85–0.97)
  - Best GLS cutoff: -18.0%
  - Sensitivity: 92%, Specificity: 85%

5. **Correlation Analysis**

Parameter Pair	Correlation Coefficient (r)	p- value
Cumulative Chemotherapy Dose vs GLS	-0.52	< 0.001
GLS vs LVEF	0.61	< 0.001

6. **Subgroup Analysis**

a. By Gender

Gender	Subclinical LVD (%)	p-value
Female	15/70 (21.4%)	0.78
Male	5/30 (16.7%)	

b. By Malignancy Type

Malignancy	Subclinical LVD (%)	p-value
Breast Cancer	14/60 (23.3%)	0.32
Others	6/40 (15.0%)	

Discussion

The current investigation, which involved 100 cancer patients receiving cardiotoxic chemotherapy, revealed that a substantial majority were female (70%), with breast cancer identified as the predominant primary malignancy, constituting 60% of all cases. This demographic pattern aligns with numerous previous research highlighting the disproportionately elevated risk of cardiotoxicity in women, especially those receiving treatment for breast cancer. The incorporation of a primarily female breast cancer cohort in this study reflects actual clinical situations where the risk of cardiotoxicity is essentially elevated due to both patient and treatment-related variables. The average baseline left ventricular ejection fraction (LVEF) in our cohort was 61.7% ± 4.3%, while the mean global longitudinal strain (GLS) was -19.5% ± 1.1%, both of which are within the recognised normative ranges for healthy persons.

It is now increasingly acknowledged that a preserved left ventricular ejection fraction (LVEF) may not necessarily indicate maintained myocardial health, particularly in the initial phases of chemotherapy-induced cardiac damage [7]. This highlights the therapeutic significance of integrating myocardial deformation imaging, such as GLS, into standard monitoring methods. GLS provides a more nuanced evaluation of subclinical myocardial failure, identifying modest contractile deficiencies prior to noticeable volumetric alterations in LVEF. The findings thus validate the use of GLS as a primary diagnostic tool for assessing cardiotoxicity risk, especially in cancer patients with normal baseline echocardiograms but significant expected exposure to cardiotoxic drugs.

Approximately 20% of patients in the current study exhibited subclinical left ventricular dysfunction (LVD), evidenced by a decrease in global longitudinal strain (GLS) to values exceeding -18% despite maintained left ventricular ejection fraction (LVEF), while 6% advanced to overt LVD, defined by a reduction in LVEF to below 50%, during the 6-month follow-up period. The moderate incidence (6%) of overt left ventricular dysfunction in our group may reflect the therapeutic advantages of early diagnosis via global longitudinal strain monitoring and the subsequent application of

preventative cardioprotective interventions such as beta-blockers or ACE inhibitors. The diminished progression rate may be ascribed to proactive cardiac screening techniques, dosage adjustments, and tight interdisciplinary collaboration between oncologists and cardiologists. The utilisation of GLS as a standard surveillance instrument allows doctors to identify myocardial injury in its early phase, before to any drop in volumetric metrics such as LVEF, thus offering a vital opportunity for therapeutic intervention.

The findings indicate a distinct and progressive reduction in global longitudinal strain (GLS) values from baseline (-19.5%) to 3 months (-18.2%) and subsequently to 6 months (-17.3%), with robust statistical significance ($p < 0.001$), underscoring the temporal pattern of myocardial deformation in patients with initially preserved cardiac function. Conversely, left ventricular ejection fraction (LVEF) demonstrated a statistically significant decrease from 61.7% to 56.8%, reflecting a very mild fall over the same period. This disparity in trends significantly supports the idea that GLS is a more sensitive and early biomarker of myocardial dysfunction than LVEF, which typically remains within the normal range until more advanced or overt cardiac damage manifests [8]. The dynamic characteristics of GLS, which measures myocardial fibre deformation instead of only volumetric output, facilitate a detailed comprehension of ventricular function, particularly in the longitudinal fibres of the subendocardial region—the area most vulnerable to chemotherapeutic damage. Since LVEF frequently remains intact until considerable myocardial impairment has transpired, dependence exclusively on LVEF may postpone identification and treatment [9].

A moderate negative correlation ($r = -0.52$, $p < 0.001$) identified in our investigation between cumulative chemotherapeutic dosage and global longitudinal strain (GLS) underscores a distinct dose-dependent association between cardiotoxic exposure and myocardial strain deterioration. As the cumulative dosage of chemotherapeutic drugs, especially anthracyclines, escalated, GLS values exhibited a gradual reduction in negativity, signifying a deterioration in cardiac deformation. Furthermore, this investigation demonstrated a modest positive connection between GLS and LVEF ($r = 0.61$, $p < 0.001$), reinforcing the notion that these two echocardiographic parameters are interconnected, but not synonymous. Although LVEF quantifies volumetric ejection and indicates overall pump performance, it frequently remains within the normal limits until substantial myocardial damage has transpired. Conversely, GLS identifies nuanced alterations in myocardial fibre shortening, especially within the subendocardial layer, which is the initial site impacted by cardiotoxic substances [10]. Consequently, GLS functions as a more sensitive and earlier marker of subclinical cardiac impairment. The relationship between GLS and LVEF indicates that decreasing strain levels may precede and maybe forecast later declines in LVEF, enabling proactive management before to the manifestation of overt systolic dysfunction [11].

The investigation of this study revealed that no statistically significant difference in the incidence of subclinical left ventricular dysfunction (LVD) between genders ($p = 0.78$) or across various cancer types ($p = 0.32$). The incidence of subclinical left ventricular dysfunction was numerically elevated in female patients and those with breast cancer, perhaps attributable to their increased representation in the study population; however, this trend lacked statistical significance, potentially due to constraints in sample size and subgroup power. A possible explanation for this divergence is because our analysis aggregated all chemotherapeutic agents instead of stratifying by individual medication class, thereby obscuring differences in cardiotoxic risk among treatment regimens.

These findings align with those from multicenter and multinational research, thereby validating our selected cutoff point and highlighting GLS as a dependable, reproducible, and quantitative instrument for evaluating cardiotoxicity. Its enhanced sensitivity renders it especially effective in oncology environments where early diagnosis is crucial for altering or ceasing potentially cardiotoxic treatment before irreparable harm transpires [12]. Moreover, its considerable specificity minimises false positives, hence decreasing the likelihood of unwarranted treatment interruptions or interventions. The efficacy of GLS, as evidenced by our ROC analysis, supports its incorporation into standard cardio-oncology monitoring protocols, especially for high-risk populations like breast cancer patients on anthracycline or trastuzumab treatments.

Conclusion

The notable association between GLS and chemotherapy dosage underscores the necessity of monitoring cumulative exposure and the potential for early intervention with cardioprotective therapies, such as beta-blockers and ACE inhibitors, as examined in research trials. The fall in GLS occurs prior to the loss in LVEF, establishing it as a more effective early diagnostic instrument for cardiotoxicity. The determined GLS cutoff of -18% is clinically significant and aligns with recognised recommendations, rendering it suitable for routine clinical application. This study establishes that GLS is a dependable and early indicator for identifying subclinical left ventricular dysfunction in cancer patients receiving cardiotoxic chemotherapy. Its enhanced sensitivity relative to LVEF, notable

connection with total chemotherapy dosage, and robust predictive accuracy underscore its use in standard cardio-oncology monitoring.

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