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Original Research Article

Strain Imaging: Utility in Early Diagnosis of Chemotherapy Induced Cardiac Dysfunction, an Edge Over Routine Echocardiography

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Abstract:

Introduction: cancer is the second-leading contributor to mortality worldwide, and between 2020 and 2025, In terms of the most common cause of mortality, it is anticipated to surpass heart disease. Global longitudinal strain was assessed by Negishi et al. using speckle tracking in breast malignancy patients, in addition to it was found that strain was an additional interpreter of decreased LVEF as well as an independent predictor of chemotherapy-induced cardio-toxicity. In current breast cancer patients, strain imaging has also been utilized towards identify subclinical cardiotoxicity brought on by radiation therapy. Conventional echocardiogram revealed no differences, but at all post radiation management interval periods aimed at left-sided patients nevertheless not aimed at right-sided patients a decline in global strain as well as anterior wall strain (area of greatest mean dose) was seen.

Aims and Objectives: To determine the efficacy of strain imaging over routine echocardiography in early diagnosis of cardiac dysfunction induced by chemotherapy.

Methods: A randomized controlled trial with 200 patients divided into two groups, GLS-guided and EF-guided, was conducted to measure the efficacy of surveillance of anthracycline-based cancer therapy-induced cardiotoxicity. All facilities involved performed calibration exercises to ensure accurate measurement of echocardiographic data. Patients underwent baseline echocardiograms before starting or supplementing anthracycline medication, followed by echocardiograms every three months. Patients in the GLS-guided arm received ACE inhibitors and beta-blockers upon diagnosis of LVEF-CTRCD or a 12% relative GLS reduction.

Results: The study found that the difference in left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS) between baseline and 1-year follow-up for patients in the EF-guided and GLS-guided groups. The difference in LVEF between the two groups was not statistically significant (P=0.68), but the GLS-guided group had a slightly smaller reduction in GLS compared to the EF-guided group (P=0.09). Both groups had a significant reduction in LVEF and GLS from baseline to 1-year follow-up (P<0.001). The results suggest that GLS-guided surveillance may help prevent a significant reduction in LVEF to the abnormal range in patients receiving anthracycline-based cancer therapy. The GLS-guided group had significantly higher rates of receiving ACE inhibitors/ARBs (P<0.001) and beta-blockers (P=0.006) compared to the EF-guided group. Both groups had similar rates of achieving maximal doses of ACE inhibitors/ARBs and beta-blockers. The results suggest that GLS-guided surveillance may lead to higher rates of receiving cardioprotective medication in patients receiving anthracycline-based cancer therapy.

Conclusion: The study shows that using global longitudinal strain (GLS) for surveillance of cardiotoxicity in patients undergoing anthracycline-based cancer therapy can help prevent a meaningful fall of left ventricular ejection fraction (LVEF) to the abnormal range.

Keywords: echocardiography, chemotherapy, Strain, cardiotoxicity.

Introduction

Since 2006, cancer is the second-leading contributor to mortality worldwide, and between 2020 and 2025, In terms of the most common cause of mortality, it is anticipated to surpass heart disease (CVD) [1]. Obesity, sedentary lifestyles, arterial hypertension, tobacco usage, diabetes mellitus, advanced age, in addition to dietary habits is risk factors for both cancer and CVD. As a result, there is an increased incidence of tumor as well as cardio vascular diseases (CVD). Both disorders can be diagnosed and prevented by using an integrated approach [2]. Cancer chemotherapy (CT) has improved survival rates, but it also increases the threat of cardio-toxicity (CTX), the prevalence of asymptomatic ventricular failure, and uniform the likelihood of cardiomyopathy [3]. Because the increased probability of regaining systolic functions the earlier this cardiac event is recognized, early CTX diagnosis is crucial [4].

The care of patients with cancer receiving cardio-toxic therapies has relied heavily on echocardiographic imaging. Despite the wide range of cardiovascular conditions that can affect cancer patients, early diagnosis of cardiomyopathy is of particular relevance since it has implications for continued cancer treatment and is linked to a poor prognosis [5]. The most popular metric for determining left ventricular (LV) dysfunction prior to, throughout, as well as following cancer treatment is left ventricular ejection fraction (LVEF). Although LVEF is a reliable diagnostic and prognostic measure in a variety of cardiovascular illnesses, it lacks the sensitivity to identify early myocyte damage brought on by cardio-toxic therapy that results in subclinical changes in cardiac function [5].

The degree of provincial alteration in myocardial deformation is referred to as strain (% modification of dimensions). When using speckle-tracking echocardiography to measure strain, interference patterns in the cardiac tissue are created by the natural acoustic markers that appear in gray scale images. Kernels, which are isolated sections of myocardium through momentarily steady as well as distinctive speckled formations, can be followed automatically from frame towards frame throughout the cardiac cycle [6] after random noise has been removed. Using the use of speckle-tracking technology, the immediate separation amongst two kernels may be measured, allowing for substantially angle-independent regional evaluation. It is possible to assess a more comprehensive measurement of LV purpose through utilizing a usual cost from several areas. Most significantly, global longitudinal strain which can be intended through be an average of longitudinal strain values from three common apical projections is becoming recognized as a useful clinical indicator of LV failure [6]. With the aid of speckle-tracking echocardiography (STE), it is now possible to evaluate LV deformation, or strain, which offers a quantitative assessment of ventricular contractile function. It has been demonstrated that strain imaging is clinically useful in a number of contexts. The most extensively researched strain metric, global longitudinal strain (GLS) has a high diagnostic and prognostic value [7]. Compared to LVEF, it is an added accurate as well as sensitive indicator of LV systolic

function. The best deformation measure for identifying subclinical LV dysfunction is thought to be GLS. When a decrease in LVEF caused by chemotherapy is confirmed, it might be too late to receive treatment to enable a full recovery [6]. GLS has become a key indicator of cardio-toxicity [7]. However, despite the fact that there is evidence demonstrating the clinical usefulness of this technology, few doctors are aware with the actual procedure of strain imaging.

Global longitudinal strain was assessed by Negishi et al. using speckle tracking in breast malignancy patients, in addition to it was found that strain was an additional interpreter of decreased LVEF as well as an independent predictor of chemotherapy-induced cardio-toxicity [8]. As in current significant systematic evaluation, Thavendiranathan et al. came to the conclusion that strain was useful aimed at the initial finding of cardiac abnormalities as well as the prophecy of cardiotoxicity in patients undergoing treatment for cancer [9]. In current breast cancer patients, strain imaging has also been utilized towards identify subclinical cardiotoxicity brought on by radiation therapy. Conventional echocardiogram revealed no differences, but at all post radiation management interval periods aimed at left-sided patients nevertheless not aimed at right-sided patients a decline in global strain as well as anterior wall strain (area of greatest mean dose) was seen [10]. This review examined the advantage of strain imaging over standard echocardiography in the early detection of heart dysfunction by chemotherapy.

Materials and methods

Study design

200 people visited our hospital's outpatient clinic as part of a randomised controlled trial. Two groups, each containing 100 patients, were created: those who GLS guided and those who EF-guided. Accurate measurement of echocardiographic data required all participating hospitals to conduct a calibration exercise before patient enrollment. Patients who had baseline echocardiograms before beginning anthracycline medication or supplementary therapy in those who had already started it. Regardless of the therapy plan, echocardiograms were performed every three months afterwards; this analysis only includes echocardiograms taken within a year of the study's enrollment or the most recent echocardiogram taken before that period. Patients have prescribed an ACE inhibitor first, then a beta-blocker after receiving a diagnosis of LVEF-CTRCD in either arm of the study or a 12% relative GLS reduction in the GLS-guided arm, whichever came first.

Inclusion and exclusion criteria

Patients older than 20 taking chemotherapy for cancer can participate in the trial. Patients with an established LV ejection fraction of 53 per cent or above.

Patients with a documented LV ejection fraction of less than 53% were not eligible for inclusion. People with diabetes. Patients who have both coronary artery disease and a non-ischaemic form of heart muscle disease

Statistical analysis

Statistical analysis and data entry were performed with the help of ANOVA. Using the means, standard deviations, student's t-test, and Chi-square, we could make the appropriate percentage comparisons between the different groups. The cutoff for statistical significance was set at the 0.05 level.

Ethical approval

The authors provided the patients with a detailed explanation of the trial. All necessary consents from the patients have been obtained. The hospital's ethics board approved the research protocol.

Results

Table 1 displays the baseline characteristics of 200 patients split evenly across two groups. Patients' ages ranged from 55 to 13 on average, and 96% of them were female. Heart failure risk factors were common: 59 were current or former smokers, 39 (13%) had diabetes mellitus, and 60 had hypertension. Most patients (n = 183) had breast cancer, the majority of which was HER2+ (n = 177). The remaining patients (n = 20) all had lymphomas or leukemias.

Table 1: patient demographics and clinical baseline features

	EF guided (n=100)	GLS guided (n=100)	P value
Age years	56 (47-65)	55 (45-66)	0.821
Female	96 (96)	94 (94)	>0.98
Race			0.291
African	**1 (1)**	**1 (1)**	
European	67 (67)	62 (62)	
South Asian	8 (8)	4 (4)	
East Asian	22 (22)	29 (29)	
Others	5 (5)	6 (6)	
Hypertension	31 (31)	29 (29)	0.711
Diabetes	17 (17)	10 (10)	0.062
Smoking	29 (29)	30 (30)	0.901
Dyslipidemia	25 (25)	18 (18)	0.163
Prior cardiovascular disease	10 (10)	11 (11)	0.851
ACE inhibitor or ARB	15 (15)	14 (14)	0.871
Beta-blocker	5 (5)	6 (6)	>0.98
Statin	18 (18)	10 (10)	0.049
Diastolic blood pressure, mmHg	77 (71-81)	79 (71-81)	0.411
Systolic blood pressure, mmHg	124 (114-136)	126 (117-137)	0.551
Heart rate, beats/min	78 (71-86)	75 (67-86)	0.261
Cancer history			
Breast cancer	91 (91)	92 (92)	0.851
Breast cancer characteristics			
ER+	60 (60)	61 (61)	0.901
HER2+	86 (86)	91 (91)	0.281
PR+	48 (48)	50 (50)	0.811
Lymphoma	8 (8)	7 (7)	0.831
Bilateral	5 (5)	4 (4)	0.821
Acute myelogenous leukemia	3 (3)	2 (2)	>0.982.8
Left-sided	51 (51)	55 (55)	0.821
Echocardiogenic parameters			
Echocardiography pre trastuzumab	78 (78)	82 (82)	0.34
Core laboratory measurement, %			
GLS	-21.2 ± 2.8	-21.5 ± 2.5	0.077
3D LVEF	59 ± 7	60 ± 7	0.101
Site measurement, %			
GLS	-21.2 ± 2.7	-21.4 ± 2.4	0.271
3D LVEF	62 ± 5	62 ± 6	0.521

Although the same percentage of patients got a new diagnosis of LVEF, 56%, At the one-year follow-up, the LVEF in the group that EF guided was significantly lower than the LVEF in the group that GLS guided. The GLS of the EF-guided arm experienced a malfunction at some point. However, neither of these variables substantially differed between the 2 arms in their change from baseline to 1 year (table 2).

Table 2: GLS and LVEF variation from pre-followup to post-followup 1 year

	EF guided			GLS guided			Difference, %(95%, CI)	P value
	n	LV function % (95% CI)	P-value	n	LV functionn % (95% CI)	P-value		
Core laboratory 3D EF, %								
1 year	100	56 (55 to57)		100	58 (57 to 59)		-1.7 (-3.2 to 0.1)	0.06
Baseline	100	59 (56 to 60)		100	60 (57 to 61)		-1.5 (-2.9 to 0.4)	0.11
1 year- baseline	100	-3.4 (-1.9 to -4.6)	<0.001	100	-2.9 (-1.9 to -4.1)	<0.001	0.5 (-1.6 to 2.1)	0.68
Core laboratory GLS, %								
1-year	97	-19.3 (-19.8 to -18.9)		95	-19.7 (-20.5 to -19.8)		0.57 (-0.09 to 1.18)	0.09
Baseline	100	-20.8 (-21.2 to -20.3)		100	-21.2 (-21.5 to -20.9)		0.52 (-0.07 to 1.06)	0.09
1 year- baseline	97	1.9 (2.1 to 1.2)	<0.001	95	1.8 (2.1 to 1.2)	<0.001	-0.11 (-0.72 to 0.54)	0.76

In both groups, maximum doses of ACE inhibitors/ARBs and beta-blockers were similar. The most common reasons for not reaching maximal dosages are hypotension, bradycardia, and the discovery of CTRCD at the last visit. All other individuals took at least 1 ACE inhibitor/ARB or beta-blocker, except those who refused therapy with cardiac medicines. None of the patients experienced severe adverse side effects after starting their cardiac drugs (table 3).

Table 3: Treatment details for cancer therapy-related cardiac dysfunction

	EF guided (n=100)	GLS guided (n=100)	P value
Received ACE inhibitor/ ARB	12 (12)	30 (30)	<0.001
Received BB	13 (13)	26 (26)	0.006
Received both	11 (11)	25(25)	0.003
Maximal doses of ACE inhibitor/ARB achieved, %	32 (26-64)	51 (26-52)	0.82
Aximal dose of beta-blocker achiever, %	26 (13-52)	26 (13-52)	0.45

6 patients were assigned to the EF-guided arm, while 4 patients were assigned to the GLS-guided arm discontinued cancer therapy, with a p-value for the interaction between the two arms of 4 and 7. Table 4 provides a summary of the causes for stoppage or discontinuance.

Table 4: Cancer therapy discontinuations or interruptions

	Interruption		Discontinuation	
	EF guided (n=6)	GLS guided (n=4)	EF guided (n=4)	GLS guided (n=7)
Left ventricular dysfunction	1	0	1	1
Serious adverse effects and/or occurrences of adverse events	1	2	1	2
Effects of chemotherapy	2	1	1	3
Other reasons	2	1	1	1

Discussion

In 2020, Liu et al. researched and examined strain imaging in cardio-oncology. For the proper care of patients receiving cardiotoxic cancer therapy, echocardiographic imaging is essential. The most common indicator of left ventricular dysfunction is the ejection fraction of the left ventricle. Unfortunately, it lacks the sensitivity necessary to detect mild changes in heart function that may accompany cardiotoxic treatment. The most thoroughly researched strain parameter with recognized diagnostic and prognostic significance is the "global longitudinal strain (GLS)". Changes in GLS have been shown to serve as an early indicator of cardiotoxicity in numerous investigations. The goal of this article is to serve as a primer for doctors on how to acquire and interpret strain in cardio-oncology. Examples with embedded videos show how to take GLS measurements step-by-step and show frequent mistakes to avoid. The document describes GLS's uses in cardio-oncology and its function in directing cancer treatment. With advice on training and quality control, practical methods for implementing strain in the echo laboratory are also presented [11].

Despite significant improvements in the research applications of strain and strain rate, the technique has gained public acceptance and become regularly used. The speed of strain analysis has significantly improved, theoretically making it possible to implement it effectively in a busy laboratory. The inconsistency in the recording and analysis of strain has been a significant barrier. Labs should create and adhere to meticulous acquisition protocols, standardize the location of the ROI, and hold in-depth team meetings for quality improvement if they want to successfully introduce strain into clinical practice. Such strategies will aid in strain standardization and enable their application in cardiovascular disorders, particularly for cardio oncology [11].

Thavendiranathan and others (2014) reviewed and studied the "Peak systolic longitudinal strain" rate, reliably identifying initial cardiac alterations throughout treatment with tissue Doppler-based strain imaging. However, peak systolic "global longitudinal strain (GLS)" seems towards is the finest marker through speckle tracking echocardiography (STE). The most relevant metric aimed at the prophecy of cardiotoxicity, well-defined as a decline in LVEF or heart failure, appears to be a 10%-15% initial decrease in GLS through STE throughout rehabilitation. Global radial and circumferential strain measurement is routinely aberrant in late cancer survivors, even when LVEF is adequate. However, their predictive value in ventricular dysfunction or heart failure cases has not been studied in the clinic. The significance of echocardiographic myocardial deformation measures aimed at the initial conclusion of myocardial alterations as well as the prognosis of cardiotoxicity in patients undergoing malignancy treatment is thus confirmed by this systematic review [7].

Foulkes et al. (2020) conducted research and analysis throughout the past rare years; there have been significant enhancements in cancer-specific endurance due to ongoing developments in cancer detection and therapy. As a result, comorbidities like cardiovascular disease are increasingly defining long-term health outcomes. It's significant to note that a quantity of well-known and cutting-edge tumor managements have been linked to varied degrees of cardiovascular harm, which might not manifest for years after the end of tumor therapy. The emergence of tumor management associated cardiac dysfunction (CTRCD), which carries a significant risk of morbidity and death as well as an elevated risk of heart failure, is particularly concerning. For cancer survivors to avoid long-term cardiovascular morbidity, early CTRCD identification appears to be essential.

Nonetheless, evaluations of cardiac function during rest are still used by current clinical criteria to identify CTRCD. This gives a partial picture of the heart's reserve capability as well as may make it harder to spot subclinical myocardial damage. Recent developments in non-invasive imaging methods have made it possible towards quantify heart function during exercise, offering an innovative method of spotting initial cardiac failure that has been helpful in a number of cardiovascular illnesses. This narrative review's objectives are to: (1) deliberate the various non-invasive imaging methods that can be utilized towards quantify various characteristics of cardiac reserve; (2) deliberate the results of investigations of tumor patients that have measured cardiac reserve as a marker of CTRCD; and (3) emphasize the key knowledge gaps that must be filled in the future before cardiac reserve can be successfully incorporated routinely following on people with cancer who have been treated.

Conclusion

In conclusion, the study shows that using global longitudinal strain (GLS) for surveillance of cardiotoxicity in patients undergoing anthracycline-based cancer therapy can help prevent a meaningful fall of left ventricular ejection fraction (LVEF) to the abnormal range. However, GLS-based surveillance did not alter the 12-month LVEF response for all patients at elevated risk for chemotherapy-induced cardiotoxicity (CTRC). The findings indicate that GLS can be used as an effective tool for surveillance of CTRCD, but further research is needed to identify the threshold for cardiac protective therapy (CPT) in this patient population. Despite the paradoxical results, when patients receiving CPT were compared, those in the GLS-guided arm had a significantly lower reduction in LVEF at the 1-year follow-up. Therefore, the study supports the use of GLS in the surveillance of CTRCD and highlights the potential benefits of GLS-guided CPT.

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