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ARTÍCULO ORIGINAL (Versión en inglés)

Evaluación prospectiva de los cambios en la deformación longitudinal global tras la radioterapia en pacientes con cáncer de mama del lado izquierdo y del lado derecho

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Resumen

Antecedentes: La radioterapia (RT) para el cáncer de mama podría asociarse con disfunción cardíaca subclínica que no puede identificarse mediante parámetros ecocardiográficos convencionales. La ecocardiografía transtorácica (ETT) utilizando la deformación longitudinal global (GLS) es un predictor valioso de disfunción miocárdica subclínica. **Objetivo:** Utilizar la ecocardiografía transtorácica con análisis de deformación longitudinal global para evaluar si las alteraciones de la deformación del ventrículo izquierdo (VI) posteriores a la radioterapia reflejan evidencia temprana de remodelado cardíaco en pacientes con cáncer de mama. **Diseño del estudio:** Estudio de cohorte. **Lugar y duración del estudio:** Este estudio prospectivo de cohorte se realizó en el Centro de Cirugía Cardíaca y Terapia Transcatéter de Al-Najaf, Hospital Docente Al-Sader, en la ciudad de Al-Najaf, desde diciembre de 2024 hasta septiembre de 2025. **Métodos:** Este estudio de cohorte incluyó a 40 mujeres con cáncer de mama, entre 20 y 65 años, que se dividieron en dos grupos: pacientes con cáncer de mama del lado izquierdo (n=18) y del lado derecho (n=22). La deformación longitudinal global del ventrículo izquierdo (LVGLS) se evaluó mediante ecocardiografía transtorácica estándar 2D antes de la radioterapia y dentro de los 10 días posteriores a la radioterapia. Para las comparaciones estadísticas se utilizaron la prueba t independiente, la prueba t pareada y la prueba ANOVA. **Resultados:** En comparación con el periodo previo a la radioterapia, la deformación longitudinal global del ventrículo izquierdo posterior a la radioterapia disminuyó significativamente (-16.34±1.44% vs. -18.09%±1.6%, p<0.001). Las pacientes con cáncer de mama del lado izquierdo presentaron una reducción significativamente mayor en la GLS del VI en comparación con las del lado derecho (-15.7%±0.9% vs. -16.9%±1.5%, p=0.006). Un índice de masa corporal (IMC) más alto se asoció con una mayor reducción de la GLS del VI. **Conclusión:** Incluso antes de la presencia de síntomas clínicos evidentes, la LVGLS es un indicador temprano de cardiotoxicidad subclínica posterior a la radioterapia en pacientes con cáncer de mama. La irradiación del lado izquierdo se asocia con una mayor reducción de la LVGLS. Los cambios tempranos en la GLS destacan la importancia de una monitorización cardíaca más estrecha en pacientes con cáncer de mama.

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Palabras clave: cáncer de mama, radioterapia, cardiotoxicidad, enfermedades cardíacas inducidas por radiación, ecocardiografía, ecocardiografía con seguimiento de *speckle*, deformación longitudinal global

Summary

Prospective Evaluation of Global Longitudinal Strain Changes Following Radiotherapy in Left-Sided and Right-Sided Breast Cancer Patients

Abstract Background: Radiotherapy (RT) for breast cancer could be associated with subclinical cardiac dysfunction that cannot be identified by conventional echocardiographic parameters. Transthoracic echocardiography (TTE) using Global longitudinal strain (GLS) is a valuable predictor of sub-clinical myocardial dysfunction. **Objective:** Using transthoracic echocardiography with global longitudinal strain analysis to evaluate whether post-radiotherapy alterations in left ventricular (LV) strain reflect early evidence of cardiac remodeling in breast cancer patients. **Study Design:** Cohort study. **Place and Duration of Study:** this prospective cohort study was conducted at Al-Najaf Center for Cardiac Surgery and Transcatheter Therapy, Al-Sader Teaching Hospital in Al-Najaf city from December 2024 to September 2025. **Methods:** This cohort study was consisted of 40 females with breast cancer between the ages of 20 and 65 years were split into two groups: left sided breast cancer patients (n=18) and right sided breast cancer patients (n=22). Left ventricular global longitudinal strain (LVGLS) Was assessed using standard 2D transthoracic echocardiography pre-radiotherapy and within10 days post-radiotherapy. Independent t-test, paired t-test and ANOVA test were used for statistical comparisons. **Results:** Compared to pre

radiotherapy, post radiotherapy left ventricular global longitudinal strain was significantly decreased (-16.34±1.44% vs.-18.09%±1.6%, p<0.001). left sided breast cancer patients had a significantly higher reduction in LV GLS compared to right sided (-15.7%±0.9% vs.-16.9%±1.5%, p=0.006). Higher body mass index (BMI) was associated with higher reduction in LV GLS. **Conclusion:** Even before the presence of obvious clinical symptoms, LVGLS is an early indicator of post radiotherapy sub clinical cardio-toxicity in breast cancer patients. Left side irritation is associated with a higher reduction in LVGLS. The early changes in GLS high light the importance of closer cardiac monitoring in breast cancer patients.

Keywords: breast cancer, radiotherapy, cardio-toxicity, radiation-induced heart diseases, echocardiography, speckle tracking echocardiography, global longitudinal strain

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Introduction

With about 2.3 million new cases and 670,000 deaths in 2022, breast cancer is the most common cancer affecting women worldwide. Approximately 1 in 20 women will be diagnosed with breast cancer in their lifetime [1]. Radiotherapy is a cornerstone of breast cancer management but cardiac exposure—mainly in left-sided breast cancer-is still a concern despite the technological improvement in radiotherapy techniques because of the risk of radiation induced heart disease (RIHD) that may lead to long term cardiac dysfunction [2, 3]. The measurement of left ventricular ejection fraction (LVEF) using conventional echocardiography had failed to recognize the subclinical cardiac dysfunction at its earliest stage [4, 5]. Global longitudinal strain (GLS) measured by speckle-tracking echocardiography has represents an efficient and accurate method for early recognition of myocardial dysfunction before obvious changes in LVEF occur. Different studies have reported persistent reductions in GLS after breast cancer radiotherapy, indicating subclinical LV remodeling despite preserved conventional echocardiography indices such as LVEF [6, 7]. The utility of GLS as a sensitive marker of subclinical myocardial impairment is supported by its application in other at-risk populations, demonstrating subclinical myocardial dysfunction using speckle tracking echocardiography, emphasizing the ability of strain imaging to uncover cardiac impairment in the absence of overt disease [8]. This study was conducted to prospectively assess GLS changes in patients with left-sided and right-sided breast cancer, with the goal of identifying whether post-RT GLS variations function as early indicators of subclinical cardiac dysfunction.

Methods

This prospective cohort study was conducted at Al-Najaf Center for Cardiac Surgery and Transcatheter Therapy, Al-Sader Teaching Hospital, Al-Najaf city, between December 2024 and September 2025. It included 40 females diagnosed with breast cancer (aged 20–65) treated with adjuvant radiotherapy. Patients were divided into two groups: right-sided breast cancer (n=22) and left-sided breast cancer (n=18). Patients aged above 65 years old, had breast cancer metastasis or other types of cancers, previous had radiotherapy to the chest and those with history of coronary artery diseases valvular disease, or arrhythmia were excluded. For each participant body weight and height were measured to calculate their BMI. Fasting blood glucose and blood pressure in addition to the presence of diabetes mellitus and hypertension had been documented. Left ventricular GLS measurements was conducted by GE vivid E95 system using two-dimensional transthoracic echocardiography speckle-tracking methods according to the British Society of Echocardiography and British Cardio-Oncology Society recommendations [9]. For each participant GLS measured before starting radiotherapy and within 10 days after ending it. A reduction in GLS from baseline for about >15% indicated subclinical LV dysfunction. Statistical analyses were done using version 26 of the Statistical Package for the Social Sciences (SPSS) software, by using paired t-test comparisons of pre and post-radiotherapy were made, while comparisons of Mean GLS% according to age, side and

co-morbidities were done by independent t-test. In comparing Mean GLS% ANOVA test was used. A p-value <0.05 was considered statistically significant.

Results

40 females with breast cancer were evaluated in this study, 55% of them were right sided (22 patients) and 45% left sided (18 patients).The mean age was 49.25±9.1years , 57.5% of patients aged below 50 years (23 patients) and 42.5% aged 50 years ad above (17 patients).14 patients were hypertensive (35%).The mean body mass index was 28.7±4.2 including 15% of patients were normal weight (6 patients),55% were overweight (22 patients) and 30% were obese (12 patients). Radiotherapy technique that used for all patients was IMRT in a dose of 40.05Gy during 14-20 sessions (Table 1).

The mean LVGS was significantly reduced post-radiotherapy compared to baseline (–18.09% ± 1.6 vs.–16.34% ± 1.44, p < 0.001) (Table 2). Left sided breast cancer patients showed significantly higher reduction in GLS post -radiotherapy compared to right sided (-15.7 ± 0.9% vs. -16.9 ± 1.5%, p = 0.006) (Table 3). Regarding differences across BMI groups normal weight participants had no significant reduction in GLS post radiotherapy (p = 0.09), while overweight and obese participants had significantly reduced GLS post-radiotherapy (p = 0.0001 and p = 0.006) consecutively. There was no statistically significant difference among the 3 BMI groups when comparing the reduction in GLS post-radiotherapy between them (p = 0.4) (Figure 1). The comparison of participants aged 50+ years and 50 < years represented no significant effect on GLS reduction (p=0.43) (Table 4) and the same finding for hypertensive vs normotensive patients there was no significant difference in GLS reduction post-radiotherapy (p=0.735) (Table 5).

Discussion

This study shows that, even when LVEF was preserved, LVGLS dropped remarkably in breast cancer patients soon after radiotherapy. these results align with the findings of previous echocardiography-based studies suggested that that GLS is a sensitive indicator of early subclinical cardiotoxicity post-RT. this reduction in GLS could explain by the myocardial remodeling associated with oxidative damage, micro vascular injury and fibrosis associated with radiotherapy. In addition, left sided irradiation was associated with higher decline in GLS than right sided, this explained by higher radiation exposure of the heart and its structures in left sided breast cancer patients[7, 10]. Although the difference in GLS reduction between BMI groups did not reach a statistically significant level, participants with higher body weight (over weight and obese) reported higher GLS reduction Such results reflect the synergistic effect of adipose tissue–mediated inflammation and radiation-induced myocardial damage [11]. We did not find age correlation to GLS reduction, this is explained by the small sample size [12]. Participants with hypertension did not show a higher reduction in GLS when compared to normotensive participants [13]. This finding may be caused by small number of hypertensive patients sub group and variation in duration of hypertension and its control in addition to the use of cardio-protective anti-hypertensive medication [14]. The study results were limited by the relatively small sample size that may affect the statistical power mainly in comparison of sub groups ,the short period of post radiotherapy follow up makes it difficult to know whether this change is persistent or temporary and the inter venders variation in addition to dependency on images quality can affect the GLS measurements.

Conclusion

For patients with breast cancer, decreased GLS measurements post-radiotherapy is an important early indicator of sub-clinical left ventricular damage that recognized before EF changes of clinical symptoms present. Higher GLS impairment occurs in life sided breast cancer radiotherapy. The use of GLS in monitoring breast cancer patients treated with radiotherapy -especially those with other cardiac risk factors- can influences early detection of radiotherapy induced heart diseases and offers the potential to use cardio-protective precautions.

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Table 1: Baseline Demographic and Clinical Characteristics of the Study Participants (n = 40)

	Subgroup	No.	%
Age group (years)	less than 50	23	57.5
	50+	17	42.5
Mean±SD	49.25±9.1		
BMICLASS	Normal	6	15
	Overweight	22	55
	Obese	12	30
Mean±SD	28.7±4.2		
Side	Left	18	45
	Right	22	55
HT	Positive	14	35
	Negative	26	65

Table 2: Pre- and Post-Radiotherapy Global Longitudinal Strain (GLS) (n = 40)

	Pre	Post	Mean difference(95%CI)	P
GLS	-18.09%±1.6%	-16.34%±1.44%	-1.75% (-2.2% to -1.3%)	<0.001

Table 3: Pre- and Post-Radiotherapy Global Longitudinal Strain (GLS) according to side of breast cancer (n = 40)

	Left	Right	Mean difference(95%CI)	P
GLS pre	-18.6%±1.6%	-17.7%±1.5%	-0.9% (-1.9% to 0.1%)	0.09
GLS post	-15.7%±0.9%	-16.9%±1.5%	1.2% (0.4% to 2.1%)	0.006

Table 4: Pre- and Post-Radiotherapy GLS according to age group of breast cancer patients (n = 40)

	<50 years(n=23)	50> (n=17)	Mean difference(95%CI)	P
GLS pre	-18.3%±1.7%	-17.9%±1.4%	-0.4% (-1.4% to 0.7%)	0.464
GLS post	-16.6%±1.6%	-16.2%±1.1%	- 0.4% (- 1.3% to 0.5%)	0.43

Table 5: Pre- and Post-Radiotherapy EF% and GLS in Hypertensive vs. Normotensive Breast Cancer Patients

	Hypertensive (n=14)	Normotensive (n=26)	Mean difference(95%CI)	P
GLS pre	-17.9%±1.3%	-18.2%±1.8%	0.3% (-0.8% to 1.3%)	0.623
GLS post	-16.5%±1.4%	-16.3%±1.5%	-0.2% (-1.1% to 0.8%)	0.735

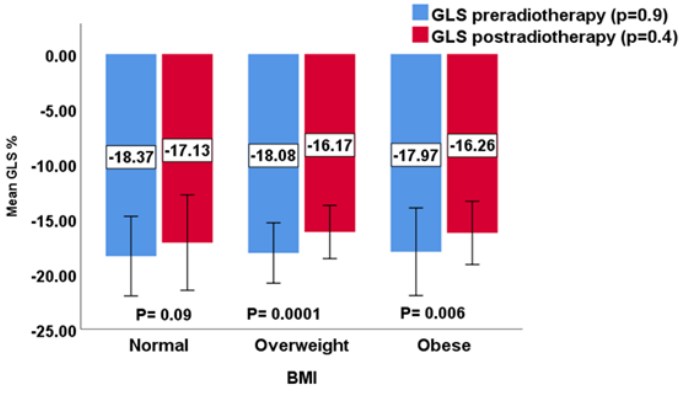

Figure 1: Changes in GLS before and after radiotherapy across BMI categories. P-values below bars represent paired t-tests; legend p-values represent between-group ANOVA comparisons