Real-world cardiotoxicity in HER2-positive breast cancer patients in Peru

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Abstract

Real-world cardiotoxicity in HER2-positive breast cancer patients in Peru. Trastuzumab improves outcomes in HER2-positive breast cancer but may cause Trastuzumab-related cardiotoxicity (TRC). Early detection is essential because LVEF often misses subclinical dysfunction, while GLS detects earlier myocardial changes. We conducted a retrospective study of 208 HER2-positive breast cancer patients treated with trastuzumab-based therapy, using institutional records from patients who received chemotherapy during April 2025. TRC was defined as a ≥10% LVEF decline to <55% or a ≥15% relative GLS reduction. TRC occurred in 17/208 patients (8.17%): 4 met TRC-LVEF and 13 met TRC-GLS criteria. This prevalence aligns with international real-world data, where 7–18% of Trastuzumab-treated patients develop cardiotoxicity and 0.4–4.5% progress to symptomatic heart failure. Hypertension was significantly associated with TRC (17.65% vs 10.99%; p=0.044), whereas age, BMI, diabetes, radiotherapy laterality, and anthracyclines were not. Anthracycline exposure differentiated the type of dysfunction, occurring in 75% of TRC-LVEF cases versus 0% of TRC-GLS cases (p=0.002), supporting that GLS detects earlier or subtler myocardial alterations not yet reflected in LVEF decline. Pertuzumab showed no significant association with TRC: 6.7% in patients without Pertuzumab vs 9.0% in those exposed (OR 1.39, p=0.61). GLS identified most TRC events (76.5%). Overall, our findings are consistent with global evidence and reinforce the need to incorporate GLS into routine surveillance to enable early detection and ensure continuity of oncologic treatment.

Introduction

Anti-HER2 therapies have significantly improved survival in HER2-positive breast cancer and are the standard of care. Early identification of Trastuzumab-related cardiotoxicity is essential to guide timely interventions and preserve cardiac function. While left ventricular ejection fraction (LVEF) remains the standard monitoring tool, it often misses subclinical dysfunction. Global longitudinal strain (GLS), derived from speckle-tracking echocardiography, offers greater sensitivity for early detection. Although Trastuzumab is used across Latin America, published data on cardiotoxicity remain limited. This study analyzes cardiotoxicity prevalence and evaluates the role of LVEF and GLS in cardiac surveillance in a real-world Peruvian cohort.

Methods and Materials

We retrospectively reviewed 208 consecutive HER2-positive breast cancer patients who received trastuzumab-based chemotherapy in April 2025. Eligible patients had complete baseline and follow-up echocardiograms with GLS measurements. TRC was defined using international consensus criteria: 1) ≥10% decline in LVEF to <55%, or 2) ≥15% relative GLS reduction from baseline. Demographic variables, clinical comorbidities, stage, radiotherapy laterality, anthracycline exposure, and pertuzumab use were collected. Statistical analyses were performed using Fisher's exact test and odds ratios with continuity correction. Forest plot was generated to visualize risk associations and characteristics distributions.

Table 1. Baseline and treatment characteristics of breast cancer patients receiving Trastuzumab

Characteristic	Total (n = 208)	Cardiotoxicity (n = 17)
Age (years)	51.20 ± 10.45 (28–86)	50.12 ± 12.21 (31–82)
BMI (kg/m²)	26.83 ± 3.94 (19–35)	27.51 ± 4.11 (21–34)
Hypertension	26 (12.50 %)	3 (17.65 %)
Diabetes mellitus	8 (3.85 %)	2 (11.76 %)
Baseline LVEF (%)	63.10 ± 4.85 (50–72)	62.41 ± 5.24 (54–71)
Final LVEF (%)	61.82 ± 5.34 (47–72)	60.93 ± 5.56 (50–70)
Stage		
Stage I	42 (20.19 %)	2 (11.76 %)
Stage II	78 (37.50 %)	6 (35.29 %)
Stage III	70 (33.65 %)	7 (41.18 %)
Stage IV	18 (8.65 %)	2 (11.76 %)
Treatment setting		
Neoadjuvant	45 (21.63 %	5 (29.41 %)
Adjuvant	86 (41.35 %)	8 (47.06 %)
Metastatic	77 (37.02 %)	4 (23.53 %)
Radiotherapy		
Left	52 (25.00 %)	5 (29.41 %)
Right	35 (16.83 %)	2 (11.76 %)
Anthracycline-based	58 (27.88 %)	5 (29.41 %)
Pertuzumab use	166 (79.81 %)	14 (82.35 %)

Results

Table 2. Risk factors in relation to Trastuzumab-related cardiotoxicity

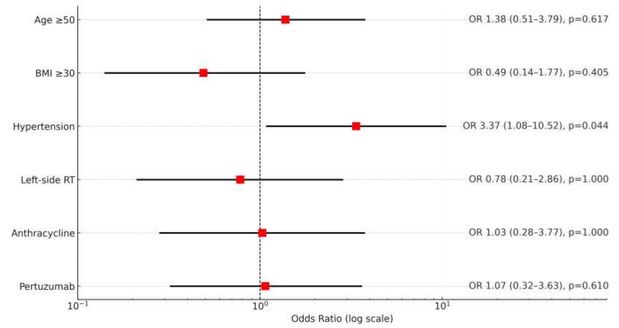
Risk factor	TRC present	TRC absent	p-Value
Age			
≥ 50 years	10	97	0.617
< 50 years	7	94	
BMI			
≥ 30 kg/m²	3	56	0.406
< 30 kg/m²	14	128	
History of diabetes			
Yes	2	6	0.132
No	15	185	
History of hypertension			
Yes	5	21	0.044
No	12	170	
Left-side radiotherapy			
Yes	3	41	1.000
No	14	150	
Prior anthracycline			
Yes	3	33	1.000
No	14	158	
Received Pertuzumab			
Yes	14	152	0.610
No	3	39	

Table 3. Trastuzumab-related cardiotoxicity patterns according to prior anthracycline exposure

TRC pattern	Anthracycline Yes	Anthracycline No	p-value
LVEF-decline TRC (n = 4)	**3**	**1**	**0.002**
GLS-decline TRC (n = 13)	**0**	**13**	

The distribution of cardiotoxicity types differed significantly according to anthracycline exposure (p = 0.002). LVEF-decline TRC was concentrated among anthracycline-treated patients, whereas GLS-decline TRC was observed exclusively in those without prior anthracycline therapy.

Figure 1. Forest plot of risk factors in relation to trastuzumab-related cardiotoxicity



Discussion

In this real-world Peruvian cohort, trastuzumab-related cardiotoxicity (TRC) occurred in 8.17% of patients, a frequency consistent with the 7–18% reported internationally. More than three-quarters of events were detected only through GLS, highlighting the limited sensitivity of LVEF for early dysfunction and reinforcing the value of strain-based surveillance. Hypertension was the only significant predictor of TRC, underscoring the importance of baseline cardiovascular risk. A striking finding was the difference in cardiotoxicity patterns: anthracycline exposure did not increase the overall incidence of TRC but was strongly associated with LVEF-decline TRC, while GLS-decline TRC occurred exclusively in anthracycline-naïve patients. This distinction suggests different trajectories of injury and supports individualized monitoring strategies.

Conclusions

Trastuzumab-related cardiotoxicity affected 8.17% of patients in this cohort, with most cases detected only by GLS. Hypertension was the main clinical predictor, and prior anthracycline exposure was closely linked to LVEF-decline TRC. These findings support routine GLS monitoring and risk-adapted surveillance based on cardiovascular comorbidities and anthracycline history.

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