Archivos de Cardiología de México

PERMANYER

Check for updates

ORIGINAL RESEARCH ARTICLE

Cardiovascular risk in cancer patients: initial experience from a cardio-oncology clinic in Mexico

Riesgo cardiovascular en cáncer: experiencia inicial de una clínica de cardiooncología en México

Cuitlahuac Arroyo-Rodríguez[1,2], Arturo E. Espinosa-Picos[2], Lorena Ledesma-Lopez[2], Marian Rodriguez-Contreras[2], Maxwell Avilés-Rodríguez[3], Jorge R. Urias-Rocha[3], Siria M. Carvajal-Lohr[3], Pamela Báez-Islas[3], Cynthia Rojas-Camarena[3], Hassan Brau-Figueroa[4], Sergio López-Portugal[3], Francisco E. Ramirez-Montoya[3], German T. Cabada-Cota[3], Julio C. Abitia-Castro[3], América Avila-Ariyoshi[5], and Enrique Avila-Monteverde[3]*

[1]Department of Cardiology, Hospital San José, Hermosillo, Son.; [2]Department of Medicine and Health Sciences, Universidad de Sonora, Hermosillo, Son.; [3]Centro de Alta Especialidad, Oncología San José, Hermosillo, Son.; [4]National Network of Cancer Registries, Instituto Nacional de Cancerología, Mexico City; [5]Fundación Tres Campanadas, Hospital San José, Hermosillo, Son. Mexico

Abstract

Objective: *To describe the cardiovascular risk from Mexican patients scheduled to initiate cancer treatment and to compare the risk between oncological and hematological malignancies.* **Methods:** *We enrolled patients referred for echocardiography before initiating cancer therapies. Left ventricular ejection fraction (LVEF) and global longitudinal strain (GLS) was evaluated. To estimate the risk for developing cancer therapy-related cardiovascular toxicity (CTR-CVT) we used the Heart Failure Association-International Cardio-Oncology Society risk score (HFA-ICOS).* **Results:** *106 patients were studied, 83% (n = 88) had an oncological, and 17% (n = 18) a hematological malignancy. Breast cancer represented 89.8% (n = 79) of the oncological and lymphoma 61.1% (n = 11) of the hematological malignancies. Patients with oncological malignancies were older (55 ± 11 vs. 46 ± 14 years; p = 0.020) and more frequently female (95.5 vs. 44.4%; p < 0.001). Metastasis was more prevalent in patients with hematological malignancies (38.9 vs. 13.6%; p = 0.011). Mean LVEF was 59.42 ± 6.36 and mean GLS was 20.26 ± 4.89. Prevalence of borderline (50-54%) and reduced LVEF (< 50%) was 4.7 and 3.8%, respectively. Abnormal GLS (< 18%) was identified in 10.4%. HFA-ICOS classified 14.7% of oncological and 10.2% of hematological malignancies in the high and very high-risk categories for developing CTR-CVT (p = 0.68).* **Conclusions:** *A high risk for developing CTR-CVT was identified in 14.2% of our population. This risk was comparable among oncological and hematological malignancies.*

Keywords: *Cardio-oncology. Global longitudinal strain. Echocardiography. Chemotherapy. Cardiotoxicity. Risk prediction.*

Resumen

Objetivo: *Describir el riesgo cardiovascular en pacientes mexicanos antes de iniciar tratamientos contra el cáncer y compararlo entre neoplasias oncológicas y hematológicas.* **Métodos:** *Se estudiaron pacientes remitidos para ecocardiografía, se evaluó la fracción de eyección ventricular izquierda (FEVI) y el strain longitudinal global (SLG). Se utilizó la escala HFA-ICOS para*

Correspondence:
Cuitlahuac Arroyo-Rodríguez
E-mail: cuitla88@hotmail.com

Date of reception: 13-04-2024
Date of acceptance: 01-07-2025
DOI: 10.24875/ACM.24000080

Available online: 11-08-2025
Arch Cardiol Mex. 2025;95(4):340-349
www.archivoscardiologia.com

estimar el riesgo de toxicidad cardiovascular relacionada a terapias contra el cáncer (CTR-CVT). **Resultados:** *Se estudiaron 106 pacientes; 83% (n = 88) presentaba una neoplasia oncológica y 17% (n = 18) una neoplasia hematológica. El cáncer de mama representó 89.8% (n = 79) de las neoplasias oncológicas y el linfoma 61.1% (n = 11) de las hematológicas. Los pacientes con neoplasias oncológicas eran de mayor edad (55 ± 11 vs. 46 ± 14 años; p = 0.020) y en mayor proporción mujeres (95.5 vs. 44.4%; p < 0.001). La metástasis fue más prevalente en neoplasias hematológicas (38.9 vs. 13.6%; p = 0.011). FEVI promedio 59.42 ± 6.36 y SLG promedio 20.26 ± 4.89. La prevalencia de FEVI limítrofe (50-54%) y reducida (< 50%) fue del 4.7 y 3.8%, respectivamente. Se identificó un SLG anormal (< 18%) en el 10.4%. Se clasificaron en alto y muy alto riesgo para desarrollar CTR-CVT al 14.7 y el 10.2% de los pacientes con neoplasias oncológicas y hematológicas, respectivamente (p = 0.68).* **Conclusiones:** *Se identificó un alto riesgo de desarrollar CTR-CVT en el 14.2% de los pacientes utilizando la puntuación de riesgo HFA-ICOS. Este riesgo fue similar en los pacientes con neoplasias oncológicas y hematológicas.*

Palabras clave: *Cardiooncología. Strain longitudinal global. Ecocardiografía. Quimioterapia. Cardiotoxicidad. Predicción de riesgos.*

Introduction

Advances in cancer treatment have led to improved survival and quality of life in a wide variety of solid tumors and hematologic malignancies[1-3]. However, cancer treatments, including chemotherapy, immune therapies, targeted agents, and radiation therapy, convey toxicities that increase the risk of cardiovascular (CV) diseases[4]. Therefore, a new discipline named cardio-oncology has emerged to allow patients with cancer to receive the best possible cancer treatments safely, minimizing cancer therapy-related cardiovascular toxicity (CTR-CVT) across the entire continuum of cancer care[5].

A broad spectrum of CTR-CVT has been identified including cardiac dysfunction/heart failure, myocarditis, vascular toxicities, hypertension, arrhythmias, and pericardial and valvular diseases[4,6-9]. Different terminologies and definitions have been previously proposed to describe the spectrum of CTR-CVT, leading to inconsistencies in diagnosis and management. Recently, the first guidelines on cardio-oncology unifying the definitions and terminology of CTR-CVT have been published[10]. In addition, these guidelines recommend baseline risk stratification before starting potentially CV-toxic anticancer therapies and provide recommendations for prevention and monitoring CV complications during and after cancer treatment.

Several prediction scores have been proposed to identify patients at risk for developing CTR-CVT[11-13]. However, these scores have been for specific cancer groups and cannot be extrapolated to other types of malignancies. The most recommended CV risk assessment tool is the Heart Failure Association-International Cardio-Oncology Society risk score (HFA-ICOS), since it has been developed for seven cardiotoxic cancer therapy classes and can be easily used in oncology and hematology services[10,14].

CV imaging plays a key role in monitoring CTR-CVT, accordingly, current guidelines recommend transthoracic echocardiography as the preferred imaging technique for the assessment of cardiac function in patients with cancer treatment, being three-dimensional (3D) echocardiography and global longitudinal strain (GLS) being the endorsed modalities[10,15,16].

In clinical practice, the lack of a baseline left ventricular ejection fraction (LVEF) poses a challenge when evaluating the likelihood of a true cancer therapy-related cardiac dysfunction (CTRCD)[4]. Moreover, information from the Mexican population is limited to case reports, pharmacogenetic studies, and children surviving cancer[17-21]. The aim of this study is to describe the baseline CV risk to develop CTR-CVT, analyze the CV risk differences between patients with oncological and hematological malignancies, and describe the echocardiographic features and clinical characteristics from a Mexican population scheduled to initiate cancer treatment.

Material and methods

Study population

We prospectively enrolled newly diagnosed cancer patients who were referred for echocardiography before initiating cancer therapies during the period June 2020-september 2023. This is a prospective cohort study conducted at Hospital San José Hermosillo, a tertiary care center with a high-specialty oncology unit in northwest Mexico. Eligibility criteria: Patients above 18 years with an expected life survival of more than 6 months, based on the treating physician's judgment, were eligible. Patients with a poor echocardiographic

window were excluded from the study. Patients with a prior history of cancer who received chemotherapy or radiotherapy were not excluded. Clinical characteristics including age, gender, CV risk factors, previous cancer treatments, and current cancer diagnosis were recollected from the clinical record. Patients were classified in the oncological and hematological groups to analyze differences among them. The baseline CV risk of the enrolled patients was assessed using the HFA-ICOS risk assessment tool (available at https://guidelines.escardio.org/), which includes specific CV risk stratification pro forma for anthracyclines, Human Epidermal growth factor Receptor 2 (HER2)-targeted therapies, vascular endothelial growth factor inhibitors, breakpoint cluster region–Abelson oncogene locus inhibitors, and multiple myeloma therapies. The baseline CV risk of these patients was classified as low/medium/high/very high based on the recommendations of the HFA-ICOS Risk Tool developed for the planned cancer drug therapy. In patients with breast cancer who were planned to receive sequential therapy with anthracyclines and HER2-targeted agents, we used the pro forma designed for HER2-targeted agents. Since this tool allows the calculation of cardiac risk without the use of cardiac biomarkers, they were entered in the calculator only where available. The oncologic treatment was determined by the responsible oncologist or hematologist.

Echocardiographic examination

A complete baseline echocardiogram was performed according to current recommendations using a Vivid-E95 machine (General Electric, Milwaukee, USA)[10,22]. All tests were performed and interpreted by a level 3 echocardiographer. For the left ventricular (LV) GLS standard, four, three, and two chamber views were used, according to the EACVI/ASE/Industry Task Force for 2D speckle tracking echocardiography[23]. Adequate tracking was visually assessed before acceptance. Radial and circumferential strain were not measured. For three-dimensional analysis, dataset acquisition for 3D images was performed using second harmonic imaging from the apical approach. During acquisition, we used the multi-slice display to ensure that the entire LV cavity was included in the dataset. Four to six consecutive electrocardiography-gated sub-volumes were acquired during breath holding to generate full-volume datasets with a minimum volume rate of 20 volumes/s[24]. Measurements of 3D LV volumes and LVEF were performed using a commercially available software package (4D AutoLVQ, GE Vingmed Ultrasound, Horten, Norway). Briefly, initialization of LV endocardial border tracing was manually performed by identifying two points on the 4-chamber view image at end-diastole and at end-systole (1 point in the middle of the mitral annulus and a second point at the LV apex). Manual editing of the semi-automatically generated endocardial contours was routinely applied to include the LV outflow tract, as well as papillary muscles and trabeculae within the LV cavity.

Statistical analysis

The Kolmogorov-Smirnov test was used to study the distribution of numerical variables. Parametric variables are expressed as mean ± standard deviation; comparison between groups was done with Student's t test or ANOVA as appropriate. Non-parametric variables are expressed as median and interquartile ranges, and comparison between groups was performed using the Wilcoxon signed-rank test. Categorical variables are summarized as percentages, and comparison between groups was done with the Chi-square test. Statistical analysis was performed using IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, N.Y., USA). Two-tailed p values with an α error < 0.05 were considered statistically significant.

Results

A summary of the baseline characteristics is presented in table 1. A total of 106 patients were studied; of these, 83% (n = 88) had an oncological and 17% (n = 18) a hematological malignancy. The mean age was 53 years and 87% were women. Breast cancer represented 89.8% (n = 79) of the oncological malignancies, 6.8% (n = 6) had colorectal cancer, and 3.4% (n = 3) had a sarcoma. Among patients with hematological malignancies, lymphoma was the most frequent type, representing 61.1% (n = 11). This group also included 16.7% (n = 3) of patients with leukemia, 16.7% (n = 3) with multiple myeloma, and 5.6% (n = 1) with plasmacytoma. Patients with oncological malignancies were older (55 ± 11 vs. 46 ± 14 years; p = 0.020) and had a greater proportion of female patients (95.5%, n = 84 vs. 44.4%, n = 8; p < 0.001). Metastasis was more frequently encountered in patients with hematological malignancies (38.9 vs. 13.6%; p = 0.011). Recurrent cancer was similar between both groups (8 vs. 11.1%; p = 0.191).

The predominant CV risk factors were hypertension and obesity, both present in 24.5% (n = 26) of the total population. Other risk factors included diabetes in

Table 1. Baseline characteristics

Variable	All patients (n = 106)	Oncological malignancies (n = 88)	Hematological malignancies (n = 18)	p
Age	53 ± 12	55 ± 11	46 ± 14	0.020
Female	92 (86.8)	84 (95.5)	8 (44.4)	< 0.001
Cancer type, n (%)				< 0.001
Colorectal	6 (5.7)	6 (6.8)	0 (0)	
Sarcoma	3 (2.8)	3 (3.4)	0 (0)	
Breast	79 (74.5)	79 (89.8)	0 (0)	
Leukemia	3 (2.8)	0 (0)	3 (16.7)	
Lymphoma	11 (10.2)	0 (0)	11 (61.1)	
Multiple myeloma	3 (2.8)	0 (0)	3 (16.7)	
Plasmocytoma	1 (0.9)	0 (0)	1 (5.6)	
Metastasis	28 (26.4)	12 (13.6)	7 (38.9)	0.011
Recurrent cancer	9 (8.5)	7 (8)	2 (11.1)	0.191
Previous cardiac conditions				0.223
Myocardial infarction	1 (0.9)	1 (1.1)	0 (0)	
Long QT syndrome	1 (0.9)	1 (1.1)	0 (0)	
Dilated cardiomyopathy	1 (0.9)	0 (0)	1 (5.6)	
Diabetes	16 (15.1)	15 (17)	1 (5.6)	0.214
Hypertension	26 (24.5)	23 (26.1)	3 (16.7)	0.394
Dyslipidemia	17 (16)	16 (18.2)	1 (5.6)	0.183
Obesity	26 (24.5)	20 (22.7)	6 (33.3)	0.340
Smoking	7 (6.6)	5 (5.7)	2 (11.1)	0.398
HFA-ICS				0.466
Low risk	61 (57.5)	51 (58)	10 (55.6)	
Medium risk	30 (28.3)	24 (27.3)	6 (33.3)	
High risk	13 (12.3)	12 (13.6)	1 (5.6)	
Very high risk	2 (1.9)	1 (1.1)	1 (4.6)	
Anthracyclines	63 (59.4)	51 (58)	12 (66.7)	0.492
HER2-targeted therapies	53 (50)	53 (60.2)	0 (0)	< 0.001
Radiotherapy	49 (46.2)	45 (51.1)	4 (22.2)	0.024

Values presented as mean ± SD or percentage.
HFA-ICOS: Heart Failure Association-International Cardio-Oncology Society risk score; HER2: human epidermal growth factor receptor 2.

15.1% (n = 16), dyslipidemia in 16% (n = 17), and smoking in 6.6% (n = 7). No significant differences between groups were found in previous cardiac conditions, diabetes, hypertension, dyslipidemia, obesity, and smoking. According to the HFA-ICOS CV toxicity risk, the majority of patients were classified in the low and medium-risk categories, 85.8% (n = 91). However, 14.2% (n = 15) of the population were classified in the high or very high-risk categories for developing CTR-CVT. No significant differences between groups were found in the HFA-ICOS CV toxicity risk. Cardiac biomarkers were available for calculation of HFA-ICOS risk only in 15% of the general population and in 50% of the cases of myeloma/plasmocytoma, where they represent a higher risk when elevated[25].

The planned anticancer therapies were anthracyclines in 59.4% (n = 63), HER2-targeted therapies in 50% (n = 53), and radiotherapy in 46.2% (n = 49) of the total population. Oncological patients were more commonly planned to receive HER2-targeted therapies (60.2 vs. 0%; p < 0.001) and radiotherapy (51.1 vs. 22.2%; p = 0.024) than patients with hematological malignancies. Anthracycline prescription was comparable among groups (58 vs. 66.7%; p = 0.492). In patients with breast cancer, 40 patients (51%) were planned to

Table 2. Echocardiographic features

Variable	All patients (n = 106)	Oncological malignancies (n = 88)	Hematological malignancies (n = 18)	p
LVEF	59.42 ± 6.36	60.00 ± 5.23	56.61 ± 9.97	0.177
LVEF method 3D Simpson	 81 (76.4) 25 (23.6)	 68 (77.3) 20 (22.7)	 13 (72.5) 5 (27.8)	0.646
LVEF < 50%	4 (3.8)	2 (2.3)	2 (11.1)	0.073
LVEF 50-54%	5 (4.7)	5 (5.7)	0 (0)	0.300
GLS	20.26 ± 4.89	20.25 ± 5.27	19.55 ± 3.65	0.600
GLS < 18%	11 (10.4)	9 (10.2)	2 (11.1)	0.911
End-diastolic volume mL/m^2	49.71 ± 11.03	48.55 ± 10.42	55.33 ± 12.45	0.042
End-systolic volume mL/m^2	19.93 ± 5.83	19.58 ± 5.98	22.15 ± 4.16	0.066
Diastolic diameter	45 (42-47)	44 (41-46)	47 (43-51.5)	0.041
Systolic diameter	29 (26.5-32)	29 (26-31)	30 (27.5-36.5)	0.516
Left atrial volume mL/m^2	31.3 ± 8.61	31.55 ± 8.72	30.11 ± 8.13	0.505
Diastolic dysfunction None Grade I Grade II	 55 (50.9) 46 (43.4) 6 (5.7)	 44 (50) 40 (45.5) 4 (4.5)	 10 (55.6) 6 (33.3) 2 (11.1)	0.420

Values presented as mean ± SD or percentage.
LVEF: left ventricular ejection fraction; 3D: three dimensional; GLS: global longitudinal strain.

receive sequential therapy with anthracyclines and HER2-targeted therapies.

Echocardiographic characteristics are presented in table 2. For the echocardiographic examination, 3D echocardiography was the most frequently method used to measure LVEF (76.4%, n = 81), followed by the Simpson method (23.6%, n = 25). LVEF was 59.42 ± 6.36 of the total population. However, non-significant differences were found between groups (60.00 ± 5.23 in oncological vs. 56.61 ± 9.97 in hematological patients; p = 0.177). A reduced (LVEF < 50%) and borderline ejection fraction (LVEF 50-54%) were present in 3.8% (n = 4) and 4.7% (n = 5) of the study population. The proportion of patients with reduced and borderline LVEF was similar between groups (2.3 vs. 11.1%; p = 0.073) and (5.7 vs. 0%; p = 0.300), respectively.

GLS was 20.26 ± 4.89 in the total population. No significant differences were found in GLS among groups (20.25 ± 5.27 vs. 19.55 ± 3.65; p = 0.600). The proportion of patients with an abnormally low GLS (absolute value < 18%) was comparable between groups (10.2 vs. 11.1%; p = 0.911).

In addition, patients with oncological malignancies had lower LV end-diastolic volumes (48.55 ± 10.42 vs. 55.33 ± 12.45; p = 0.042) and smaller diastolic diameters (44 vs. 47mm; p = 0.041). This is mainly explained by a greater proportion of female patients in the oncological group. Non-significant differences were found in LV end-systolic volumes and diameters between groups (19.58 ± 5.98 vs. 22.15 ± 4.16; p = 0.066) and (29 vs. 30; p = 0.505), respectively. Furthermore, non-significant differences were found in left atrial volume (31.55 ± 8.72 in oncological vs. 30.11 ± 8.13 mL/m^2 in hematological patients; p = 0.505). Grade I diastolic dysfunction was present in 45.5% (n = 40) of oncological and 33.3% (n = 6) of hematological patients. A grade II diastolic dysfunction (reflecting high filling pressures) was also comparable among groups (4.5 vs. 11.1%; p = 0.420).

Tables 3 and 4 present the baseline characteristics and echocardiographic features according to cancer type. Of note, patients with sarcoma, multiple myeloma, and plasmacytoma had a higher prevalence of metastasis (p < 0.001). Obesity was more frequent in patients with sarcoma, lymphoma, and multiple myeloma

Table 3. Baseline characteristics according to cancer type

Variable	Breast	Sarcoma	Colorectal	Lymphoma	Leukemia	Multiple myeloma	Plasmocytoma	p
Age	55 ± 10	41 ± 12	59 ± 21	48 ± 13	29 ± 10	56 ± 8	48	0.001
Female	79 (100)	1 (33.3)	4 (66.7)	6 (54.5)	1 (33.3)	1 (33.3)	0 (0)	< 0.001
Metastasis	7 (8.9)	3 (100)	2 (33.3)	4 (36.4)	0 (0)	2 (66.7)	1 (100)	< 0.001
Recurrent cancer	6 (7.6)	0 (0)	1 (16.7)	2 (18.2)	0 (0)	0 (0)	0 (0)	0.827
Diabetes	14 (17.7)	1 (33.3)	0 (0)	1 (9.1)	0 (0)	0 (0)	0 (0)	0.758
Hypertension	21 (26.6)	1 (33.3)	1 (16.7)	2 (18.2)	0 (0)	0 (0)	1 (100)	0.559
Dyslipidemia	16 (20.3)	0 (0)	0 (0)	1 (9.1)	0 (0)	0 (0)	0 (0)	0.664
Obesity	16 (20.3)	3 (100)	1 (16.7)	5 (45.5)	0 (0)	1 (33.3)	0 (0)	0.027
Smoking	5 (6.3)	0 (0)	0 (0)	1 (9.1)	1 (33.3)	0 (0)	0 (0)	0.794
HFA-ICOS Low risk Medium risk High risk Very high risk	 46 (58.2) 21 (26.6) 11 (13.9) 1 (1.3)	 1 (33.3) 2 (66.7 0 (0) 0 (0)	 4 (66.7) 1 (16.7) 1 (16.7) 0 (0)	 5 (45.5) 4 (36.4) 1 (9.1) 1 (9.1)	 3 (100) 0 (0) 0 (0) 0 (0)	 2 (66.7) 1 (33.3) 0 (0) 0 (0)	 0 (0) 1 (100) 0 (0) 0 (0)	0.837
Anthracyclines	48 (60.8)	3 (100)	0 (0)	10 (90.9)	2 (66.7)	0 (0)	0 (0)	< 0.001
HER2-targeted therapies	52 (65.8)	0 (0)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)	< 0.001
Radiotherapy	40 (50.6)	2 (66.7)	3 (50)	3 (27.3)	0 (0)	1 (33.3)	0 (0)	0.832

Values presented as mean ± SD or percentage.
HFA-ICOS: Heart Failure Association-International Cardio-Oncology Society risk score; HER2: human epidermal growth factor receptor 2.

(p = 0.027). No significant differences were found in the risk estimation for developing CTR-CVT according to cancer type utilizing the HFA-ICOS pro forma according to cancer type. As expected, end-diastolic/systolic volumes and diastolic diameters were significantly smaller in patients with breast cancer, given a greater proportion of female patients in this group. No significant differences were found in LVEF or GLS according to cancer type.

Discussion

This study provides the baseline clinical characteristics, echocardiographic features, and CV risk profile of a Mexican population scheduled to initiate cancer treatment (Fig. 1). Our main findings can be summarized as follows: (1) The majority of patients referred for echocardiography before starting cancer therapies were female gender (87%), being breast cancer the most frequent type among them (85.9%), (2) most of the patients had a low or medium risk to develop CTR-CVT; however, 14.2% were classified in the high or very high-risk categories according to the HFA-ICOS CV toxicity risk score, (3) the risk to develop CTR-CVT was comparable among patients with oncological and hematological malignancies according to the HFA-ICOS pro forma, and (4) considering low GLS and a low and borderline LVEF, 10.4 and 8.5%, of our patients (respectively) face a higher risk for developing CTR-CVT.

The optimal time to consider CV prevention strategies in patients with cancer is at the time of cancer diagnosis and before the initiation of cancer treatment[5,10]. The HFA-ICOS CV toxicity risk score is a baseline CV risk stratification pro forma that can be used specifically to stratify risk in cancer patients before starting potentially cardiotoxic cancer therapies[14]. This tool has been validated in a wide variety of oncological and hematological malignancies[26-31]. Accordingly, patients identified in the high and very high-risk categories require a cardiology referral (preferentially a cardio-oncologist), while patients in the low-risk category should proceed to anticancer therapy without delay[10]. Patients identified at risk should receive aggressive management of CV risk factors and pre-existing CV disease. A multidisciplinary team

Table 4. Echocardiographic features according to cancer type

Variable	Breast	Sarcoma	Colorectal	Lymphoma	Leukemia	Multiple myeloma	Plasmocytoma	p
LVEF	60 ± 5	55 ± 3	60 ± 6	55 ± 12	57 ± 3	60 ± 3	62	0.220
LVEF method 3D Simpson	 61 (77.2) 18 (22.8)	 3 (100) 0 (0)	 4 (66.7) 2 (33.3)	 7 (63.6) 4 (36.4)	 2 (66.7) 1 (33.3)	 3 (100) 0 (0)	 1 (100) 0 (0)	0.723
LVEF < 50%	2 (2.5)	0 (0)	0 (0)	2 (18.2)	0 (0)	0 (0)	0 (0)	0.298
LVEF 50-54%	4 (5.1)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.352
GLS	20.2 ± 5.5	19.7 ± 4	21.2 ± 2.4	19.3 ± 4.4	18.1 ± 0.1	20.9 ± 2.8	22.5	0.969
GLS < 18%	8 (10.1)	1 (33.3)	0 (0)	2 (18.2)	0 (0)	0 (0)	0 (0)	0.686
End diastolic volume mL/m^2	47.3 ± 8.7	52.3 ± 3.2	63.5 ± 20	53.8 ± 3.9	58 ± 5.3	61.7 ± 13.6	45	0.001
End systolic volume mL/m^2	18.9 ± 5.3	23.3 ± 3.2	25.8 ± 10.1	20.3 ± 2.1	24.6 ± 2.1	25 ± 6.6	17	0.025
Diastolic diameter	43.9 ± 3.7	43.7 ± 5.1	42.3 ± 7.5	48.2 ± 7	45.7 ± 2.5	49.3 ± 5.5	40	0.026
Systolic diameter	29.2 ± 3.8	30 ± 5.6	28.3 ± 6.5	32.9 ± 10.6	30.7 ± 4	33.7 ± 4	28	0.300
Left atrial volume mL/m^2	30.9 ± 8.1	35.6 ± 3.2	38 ± 14.8	30.6 ± 6.9	24.3 ± 1.2	36.3 ± 13.8	23	0.198
Diastolic dysfunction None Grade I Grade II	 40 (50.6) 35 (44.3) 4 (5.1)	 1 (33.3) 2 (66.7) 0 (0)	 3 (50) 3 (50) 0 (0)	 6 (54.5) 4 (36.4) 1 (9.1)	 2 (66.7) 0 (0) 1 (33.3)	 1 (33.3) 2 (66.7) 0 (0)	 1 (100) 0 (0) 0 (0)	0.722

Values presented as mean ± SD or percentage.
LVEF: left ventricular ejection fraction; 3D: three dimensional; GLS: global longitudinal strain.

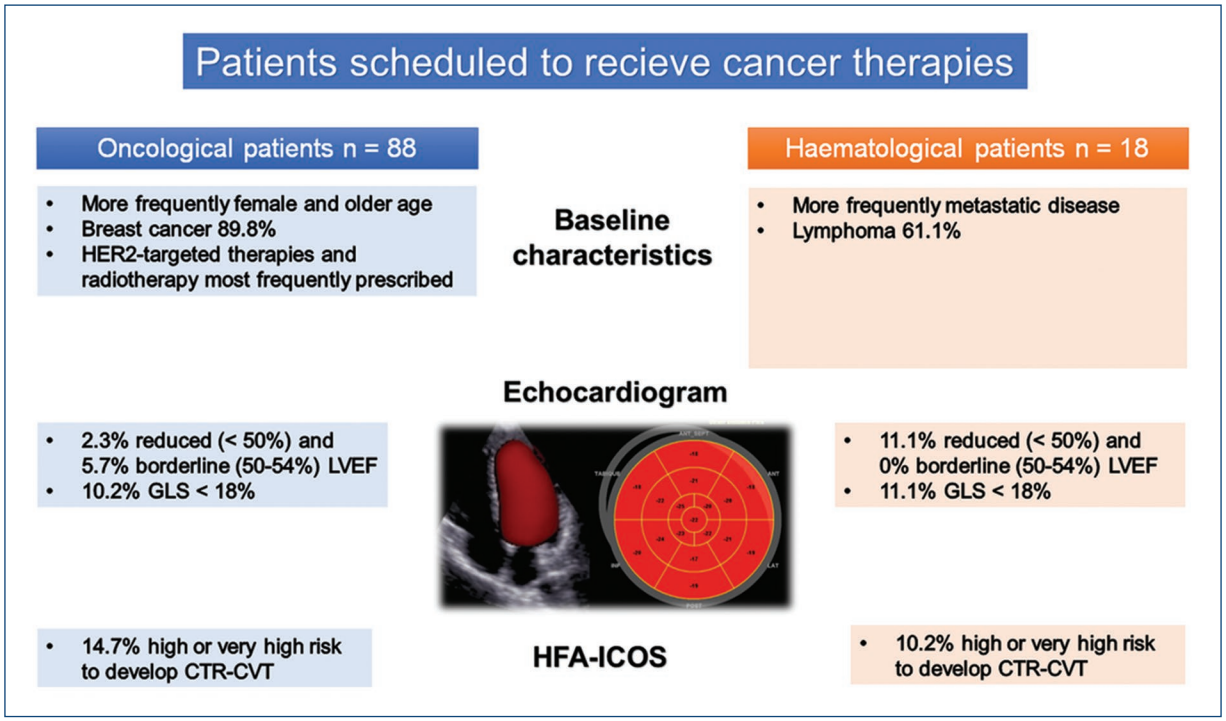

Figure 1. Patients scheduled to receive cancer therapies. HFA-ICOS: Heart Failure Association-International Cardio-Oncology Society risk score; HER2: human epidermal growth factor receptor 2. LVEF: left ventricular ejection fraction; GLS: global longitudinal strain; CTR-CVT: cancer therapy-related cardiovascular toxicity.

discussion between oncologists and cardiologists to balance the risk/benefit of cardiotoxic anticancer treatment before starting treatment in high and very-high-risk patients is recommended. There is moderate evidence supporting the use of neurohormonal blockade (angiotensin converting enzyme inhibitors or angiotensin receptor blockers and beta-blockers), statins, dexrazoxane, and liposomal anthracyclines for primary prevention of cancer therapy-related CV toxicity in high and very high risk patients[10,32].

An Italian registry of 373 patients with breast cancer identified 10.2% of their population at high or very high risk for developing CTR-CVT utilizing the HFA-ICOS risk tool. A higher proportion of patients at medium or high risk received cardioprotective agents ($p < 0.0001$), likely explaining the lack of LV dysfunction events in patients receiving anthracyclines[28]. Similar to our results, in the CARDIOTOX registry, 15.2% of patients were classified in the high or very high-risk categories. In their study, the HFA-ICOS demonstrated a good ability to predict both all-cause mortality and CV toxicity[29]. A United Kingdom study of 931 patients with breast cancer reported 8.1% of their population in the high or very high-risk categories from the HFA-ICOS score, also demonstrating increased rates of cardiotoxicity with increasing HFA-ICOS scores (14.0% low, 16.7% medium, 30.3% high/very high; $p = 0.002$)[33]. In a Japanese registry including 486 patients with hematological malignancies and breast cancer, 31.3% of their population were in the high and very-high categories of the HFA-ICOS score. Compared with the low risk category, the HR for presenting heart failure/LV dysfunction was 3.57 (95% CI 1.70-7.51, $p < 0.001$)[34]. However, the HFA-ICOS pro forma has been able to identify only the highest risk patients, and there is an ongoing need for accurate CTRCD risk prediction models in women with HER2+ breast cancer[35].

Although in our study the risk for developing CTR-CVT was comparable among patients with oncological and hematological malignancies according to the HFA-ICOS pro forma, in a recent validation of the HFA-ICOS risk score, the proportion of patients classified in the high and very-high risk categories for developing CTR-CVT was higher in hematological than oncological malignancies (27.3 vs. 9.5%)[31]. In line with this, the HFA-ICOS baseline risk score classified in the high and very high risk categories 32.4% of patients with chronic myeloid leukemia treated with nilotinib and 8.1% of patients with HER2+ breast cancer[33,36]. Moreover, in the Kurume-Creo registry, a near 2-year follow-up study demonstrated that CV adverse events were more frequent in patients with hematological malignancies than in patients with breast cancer with a good prediction ability of the HFA-ICOS proforma[34]. These disparities could be partially explained by different cancer treatment regimens, demographics, patient-related CV risk factors, as well as previous use of cardiotoxic agents[14]. In our study, a small sample size and a relatively younger population among hematological patients likely contributed to obtain similar CV risk profiles according to the HFA-ICOS pro forma.

The current definition of CTRCD involves a decline in LVEF, GLS, and a new rise in troponin or natriuretic peptides, even without symptoms of heart failure (asymptomatic CTRCD). However, patients may need heart failure therapy or hospitalization according to the severity of symptoms (symptomatic CTRCD)[4,10]. A baseline echocardiographic examination is of utmost importance to identify a true CTRCD, since some patients may have a pre-existing cardiac condition that may be misconsidered as a CTRCD leading to unnecessary interruptions or discontinuation of cancer therapies that may affect their prognosis. A baseline borderline (50-54%) or a reduced (< 50%) LVEF is a risk factor for future CTR-CVT from most cardiotoxic cancer therapies, in particular with anthracyclines or trastuzumab. Considering this, 4.7 and 3.8% of our patients had a borderline or reduced LVEF, respectively.

Furthermore, an abnormal baseline GLS can predict LV dysfunction in patients receiving anthracyclines and/or trastuzumab[10,37,38]. A cut off < 18% in GLS (absolute value) was associated with a hazard ratio of 3.54 for developing CTRCD. In our study, 10.4% of the studied population had a GLS < 18%, reflecting a higher risk population.

Limitations

First, this is a single-center observational study. Another limitation is that selection bias cannot be excluded since patients were sent to echocardiography at the discretion of the treating oncologist or hematologist (mainly in candidates to receive anthracyclines or HER2-targeted therapies). However, to the best of our knowledge, besides conference abstracts, this is the biggest cardio-oncology registry of Mexican patients, adding a missing piece of the puzzle to the literature from an under-represented population[39]. Finally, although the HFA-ICOS pro forma allows a risk calculation without cardiac serum biomarkers, this may underestimate the risk of our study population since they were not measured in the majority of our patients.

Conclusions

A high risk for developing cardiac therapy-related CV toxicity was identified in 14.2% of our population. This risk was comparable among oncological and hematological malignancies. Considering low and borderline LVEF, 8.5% of our population pose a higher risk for developing cardiac therapy-related CV toxicity. An abnormally low baseline GLS (< 18%) was identified in 10.4%, also linked to a higher risk. A close follow-up with a multidisciplinary approach is necessary in this group of patients to minimize the risk, for a prompt identification and treatment of CTR-CVT.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of interest

All authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The study was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Caswell-Jin JL, Plevritis SK, Tian L, Cadham CJ, Xu C, Stout NK, et al. Change in survival in metastatic breast cancer with treatment advances: meta-analysis and systematic review. JNCI Cancer Spectr. 2018;2:pky062.
2. Ehrhardt MJ, Krull KR, Bhakta N, Liu Q, Yasui Y, Robison LL, et al. Improving quality and quantity of life for childhood cancer survivors globally in the twenty-first century. Nat Rev Clin Oncol. 2023;20:678-96.
3. Pulte D, Jansen L, Brenner H. Changes in long term survival after diagnosis with common hematologic malignancies in the early 21st century. Blood Cancer J. 2020;10:56.
4. Herrmann J, Lenihan D, Armenian S, Barac A, Blaes A, Cardinale D, et al. Defining cardiovascular toxicities of cancer therapies: an international cardio-oncology society (IC-OS) consensus statement. Eur Heart J. 2022;43:280-9.
5. Lancellotti P, Suter TM, López-Fernández T, Galderisi M, Lyon AR, Meer PV, et al. Cardio-oncology services: rationale, organization, and implementation. Eur Heart J. 2019;40:1756-63.
6. Ewer MS, Hoff DD, Benjamin RS. A historical perspective of anthracycline cardiotoxicity. Heart Fail Clin. 2011;7:363-72.
7. Fanous I, Dillon P. Cancer treatment-related cardiac toxicity: prevention, assessment and management. Med Oncol. 2016;33:84.
8. Herrmann J. Vascular toxic effects of cancer therapies. Nat Rev Cardiol. 2020;17:503-22.
9. Melo MD, Paiva MG, Santos MV, Rochitte CE, Moreira VD, Saleh MH, et al. Posicionamento brasileiro sobre o uso da multimodalidade de imagens na cardio-oncologia - 2021. Arq Bras Cardiol. 2021;117:845-909.
10. Lyon AR, López-Fernández T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, et al. 2022 ESC guidelines on cardio-oncology developed in collaboration with the European hematology association (EHA), the European society for therapeutic radiology and oncology (ESTRO) and the international cardio-oncology society (IC-OS). Eur Heart J. 2022;43:4229-361.
11. Abdel-Qadir H, Thavendiranathan P, Austin PC, Lee DS, Amir E, Tu JV, et al. Development and validation of a multivariable prediction model for major adverse cardiovascular events after early stage breast cancer: a population-based cohort study. Eur Heart J. 2019;40:3913-20.
12. Ezaz G, Long JB, Gross CP, Chen J. Risk prediction model for heart failure and cardiomyopathy after adjuvant trastuzumab therapy for breast cancer. J Am Heart Assoc. 2014;3:e000472.
13. Romond EH, Jeong JH, Rastogi P, Swain SM, Geyer CE Jr., Ewer MS, et al. Seven-year follow-up assessment of cardiac function in NSABP B-31, a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel (ACP) with acp plus trastuzumab as adjuvant therapy for patients with node-positive, human epidermal growth factor receptor 2-positive breast cancer. JCO. 2012;30:3792-9.
14. Lyon AR, Dent S, Stanway S, Earl H, Brezden-Masley C, Cohen-Solal A, et al. baseline cardiovascular risk assessment in cancer patients scheduled to receive cardiotoxic cancer therapies: a position statement and new risk assessment tools from the cardio-oncology study group of the heart failure association of the European society of cardiology in collaboration with the international cardio-oncology society. Eur J Heart Fail. 2020;22:1945-60.
15. Plana JC, Thavendiranathan P, Bucciarelli-Ducci C, Lancellotti P. Multi-modality imaging in the assessment of cardiovascular toxicity in the cancer patient. JACC Cardiovasc Imaging. 2018;11:1173-86.
16. Guan Y. Valor diagnóstico de parâmetros tridimensionais de strain de imagem de speckle tracking para detecção de disfunção cardíaca relacionada à quimioterapia do câncer: uma metanálise. Arq Bras Cardiol. 2023;120:e20220370.
17. Siller-Nava JL, Espejel-Guzman A, Serrano-Roman J, Cabello-Ganem A, Alexis D, Ortiz A. Long term follow-up of cardiotoxicity in breast cancer treatment: a case report. WJCD. 2023;13:130-7.
18. Gándara-Mireles JA, Lares-Asseff I, Espinoza EA, Blanco JG, Font AE, Hurtado LP, et al. Association of genetic polymorphisms NCF4 rs1883112, CBR3 rs1056892, and ABCC1 rs3743527 with the cardiotoxic effects of doxorubicin in children with acute lymphoblastic leukemia. Pharmacogenet Genomics. 2021;31:108-15.
19. Avilés A, Arévila N, Maqueo JC, Gomez T, Garcia R, Nambo MJ. Late cardiac toxicity of doxorubicin, epirubicin, and mitoxantrone therapy for Hodgkin's disease in adults. Leuk Lymphoma. 1993;11:275-9.
20. Rivas-Ruiz R, Ureña-Wong K, Castelán-Martínez OD, Betanzos-Cabrera Y, Lazo-Cárdenas C, Ramírez-Portillo CR. Predictors of anthracycline-induced cardiotoxicity in a retro-prolective cohort of children surviving cancer. Gac Med Mex. 2023;156:217-23.
21. Jiménez-Carbajal MG, Antúnez-Sánchez SP, Arreguín-González FE, Benito-Reséndiz AE. Evaluación cardiovascular de pacientes sometidos a tratamientos oncológicos en una clínica de supervivientes de cáncer infantil en México. ACM. 2021;91:4207.
22. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr. 2015;28:1-39.e14.
23. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R, et al. Definitions for a common standard for 2d speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry task force to standardize deformation imaging. Eur Heart J Cardiovasc Imaging. 2015;16:1-11.
24. Lang RM, Badano LP, Tsang W, Adams DH, Agricola E, Buck T, et al. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. J Am Soc Echocardiogr. 2012;25:3-46.
25. Pavo N, Cho A, Wurm R, Strunk G, Krauth M, Agis H, et al. N-terminal B-type natriuretic peptide (NT-proBNP) is associated with disease severity in multiple myeloma. Eur J Clin Invest. 2018;48:e12905.
26. Di Lisi D, Madaudo C, Alagna G, Santoro M, Rossetto L, Siragusa S, et al. The new HFA/ICOS risk assessment tool to identify patients with chronic myeloid leukaemia at high risk of cardiotoxicity. ESC Heart Fail. 2022;9:1914-9.
27. Parra DL, Galvan JB, Alvarez RC, Estrada MC. The utility of the HFA-ICOS cardiotoxicity risk assessment tool for HER2-targeted cancer therapies in patients with metastatic breast cancer: from theory to clinical practice. Eur Heart J. 2023;44:ehad655.2712.

28. Tini G, Cuomo A, Battistoni A, Sarocchi M, Mercurio V, Ameri P, et al. Baseline cardio-oncologic risk assessment in breast cancer women and occurrence of cardiovascular events: the HFA/ICOS risk tool in real-world practice. Int J Cardiol. 2022;349:134-7.
29. Santana BR, Codon JC, Olmos JV, Monzonis AM, Zatarain-Nicolas E, Moliner P, et al. HFA-ICOS cardiovascular toxicity risk score validation in CARDIOTOX registry. Eur Heart J. 2022;43:ehac544.2591.
30. Rashed ER, Margulies KB. New cardiotoxicity risk assessment guidelines searching for validation. JACC CardioOncol. 2023;5:638-40.
31. Rivero-Santana B, Saldaña-García J, Caro-Codón J, Zamora P, Moliner P, Monzonis AM, et al. Anthracycline-Induced cardiovascular toxicity: validation of the heart failure association and international cardio-oncology society risk score. Eur Heart J. 2025;46:273-84.
32. Moreno-Arciniegas A, Cádiz L, Galán-Arriola C, Clemente-Moragón A, Ibáñez B. Cardioprotection strategies for anthracycline cardiotoxicity. Basic Res Cardiol. 2024;120:71-90.
33. Battisti NM, Andres MS, Lee KA, Ramalingam S, Nash T, Mappouridou S, et al. Incidence of cardiotoxicity and validation of the heart failure association-international cardio-oncology society risk stratification tool in patients treated with trastuzumab for her2-positive early breast cancer. Breast Cancer Res Treat. 2021;188:149-63.
34. Shibata T, Nohara S, Morikawa N, Shibao K, Ito S, Shibata R, et al. Cardiovascular adverse events and prognosis in patients with haematologic malignancies and breast cancer receiving anticancer agents: kurume-CREO Registry insights. Eur J Pre Cardiol. 2023;30:1941-9.
35. Suntheralingam S, Fan CP, Calvillo-Argüelles O, Abdel-Qadir H, Amir E, Thavendiranathan P. Evaluation of risk prediction models to identify cancer therapeutics related cardiac dysfunction in women with HER2+ breast cancer. J Clin Med. 2022;11:847.
36. Fernando F, Andres MS, Claudiani S, Kermani NZ, Ceccarelli G, Innes AJ, et al. Cardiovascular events in CML patients treated with nilotinib: validation of the HFA-ICOS baseline risk score. Cardiooncology. 2024;10:42.
37. Araujo-Gutierrez R, Chitturi KR, Xu J, Wang Y, Kinder E, Senapati A, et al. Baseline global longitudinal strain predictive of anthracycline-induced cardiotoxicity. Cardiooncology. 2021;7:4.
38. Mousavi N, Tan TC, Ali M, Halpern EF, Wang L, Scherrer-Crosbie M. Echocardiographic parameters of left ventricular size and function as predictors of symptomatic heart failure in patients with a left ventricular ejection fraction of 50-59% treated with anthracyclines. Eur Heart J Cardiovasc Imaging. 2015;16:977-84.
39. Sadler D, Arnold A, Herrmann J, Daniele A, Silva CM, Ghosh AK, et al. Reaching across the aisle: cardio-oncology advocacy and program building. Curr Oncol Rep. 2021;23:64.