

Optimization of Cardiorespiratory Fitness and Quality of Life in Women with Chronic Heart Failure after a Cardiac Rehabilitation Program

Erik E. Briceño-Gómez¹, Jorge A. Lara-Vargas², Hugo A. Radillo-Alba³, José L. Martínez-Paniagua⁴

^{1,2,3,4}Department of cardiac rehabilitation, Centro Médico Nacional "20 de Noviembre" /Universidad La Salle México. Mexico City, Mexico.

ABSTRACT

Introduction: Women with heart failure (HF) tend to experience a greater symptom burden and lower quality of life, possibly due to phenotypic differences and unique gender-associated risk factors. Despite evidence on the effects of cardiac rehabilitation programs (CRP) in the general population, there is underrepresentation of women in these programs. Additionally, the impact of CRP on cardiorespiratory variables obtained through cardiopulmonary exercise testing (CPET) and health-related quality of life (HRQoL) in women with HF remains unknown.

Objective: To assess the impact of a CRP on cardiorespiratory fitness (CRF) in cardiorespiratory variables obtained through CPET and HRQoL in women with HF.

Methods: A quasi-experimental study included HF patients who completed a CRP from June 2019 to December 2023. The CRP involved nutritional assessment, psychosocial evaluation, educational sessions, and concurrent training. It comprised 30 minutes of aerobic resistance training at 65-80% of heart rate reserve (HRR) and 30 minutes of strength training at 30-50% of 1-repetition maximum (1RM), with a frequency of 3 sessions per week for 4 to 6 weeks. CPET was conducted at the beginning and end of the program, analyzing cardiorespiratory variables. HRQoL was assessed using the SF-36 questionnaire. Gains in CRF and HRQoL at the end of the program in both men and women were analyzed.

Results: Out of 217 included patients, 29.9% were women. At the program's onset, women showed lower exercise tolerance than men (workload 5.4 ± 2.57 METs vs. 6.62 ± 2.53 METs) and worse HRQoL (62.03 ± 18.37 vs. 68.38 ± 18.37). However, post-intervention, they optimized their CRF (% predicted VO_2 [% VO_2p] initial 56.62 ± 20.11 vs final 80.12 ± 30.32 , $p < 0.001$). Significant improvements in cardiorespiratory variables were observed in both cases: delta METs-load 3.02, $p < 0.001$, delta peak oxygen consumption (VO_2peak) 1.83 ml/kg/min, $p < 0.001$, delta oxygen pulse (PO_2) 1.21, $p = 0.021$, delta cardiac power output (CPO) 1917, $p = 0.004$, with a rightward shift in ventilatory thresholds and improvement in HRQoL (62.03 ± 18.37 vs. 78.81 ± 12.9 , $p < 0.001$) post-CRP. The only variable with no significant changes in either case was VE/VCO_2 slope (delta -0.51, $p = 0.736$). Additionally, in women with reduced left ventricular ejection fraction ($< 50\%$), variables with no significant improvement included CPO (delta 959.22, $p = 0.283$) and time to recovery of VO_2 kinetics (TRC VO_2) (delta -0.74, $p = 0.957$). In patients with preserved left ventricular ejection fraction ($\geq 50\%$), variables with no significant change included PO_2 (delta 1.08, $p = 0.173$), TRC VO_2 (delta 26.82, $p = 0.099$), and the first ventilatory threshold (VT1) (delta 0.09, $p = 0.504$). Program attendance was 87.5% in both groups.

Conclusion: Implementing a CRP in women with HF resulted in significant improvements in all evaluated cardiorespiratory variables (except for VE/VCO_2 slope) and quality of life. These findings support the importance of ensuring women's access and participation in cardiac rehabilitation programs. Addressing existing barriers is crucial to maximize the long-term benefits of CRP in the female population with HF.

KEYWORDS: cardiac rehabilitation, women, cardiopulmonary exercise test, cardiorespiratory fitness, health-related quality of life.

ARTICLE DETAILS

Published On:
13 March 2024

Available on:
<https://ijmscr.org/>

Optimization of Cardiorespiratory Fitness and Quality of Life in Women with Chronic Heart Failure after a Cardiac Rehabilitation Program

INTRODUCTION

Heart failure (HF) is a multifactorial syndrome affecting various aspects of an individual, with high incidence and prevalence, currently considered a pandemic. It poses a challenge for any healthcare system due to the morbidity, mortality burden, and associated costs. It is estimated that its prevalence will exceed 8 million in the United States population by 2030 (1). In women, from 2015 to 2018, HF represented the leading cause of hospitalization, morbidity, and mortality, with up to 44,958 deaths attributed to HF in 2020 in the United States (2,3). HF can be classified based on ventricular function as reduced (HFrEF, $\leq 40\%$), mildly reduced (HFmrEF, 41-49%), or preserved (HFpEF, $\geq 50\%$) (4,5).

Regardless of ventricular function, women with HF often experience a higher symptom burden, worse health status, and lower quality of life. This may be attributed to unique gender-associated risk factors such as adverse outcomes in pregnancy and early menopause, linked to a high risk of HF (6,7), as well as endothelial dysfunction due to altered nitric oxide signaling (6). Additionally, genotypic differences contribute to women having a phenotype with a higher percentage of fat and lower lean muscle mass, leading to increased symptomatic burden related to HF and reduced exercise tolerance due to peripheral limitations (8,9). Moreover, the clinical presentation of HF in women may differ from men, exhibiting a more pronounced clinical expression despite later onset, better left ventricular function, lower prevalence of ischemic origin (6), and worse prognosis compared to the male population (7).

Regarding HF treatment, there is a deficiency in discerning if women respond similarly to men, mainly due to the limited number of women included in large clinical trials (10). Recently, CRP have been considered as an additional pillar in HF management alongside pharmacological treatment (11). This consideration is based on evidence showing a significant improvement in exercise tolerance, a reduction in hospitalizations, an improvement in quality of life, and a trend, though not statistically significant so far, in reducing mortality (12-15).

Despite being cost-effective, CRP, especially in the female population, are underutilized (16,17) due to various barriers in the referral system, program entry, adherence, and completion (18,19).

In response to these challenges, efforts have been made to facilitate specific access for women to CRP, aiming to improve cardiac functional capacity, leading to better clinical outcomes and improved functional status reflecting a higher quality of life (18-20). While studies have analyzed adaptive gains in workload (METs) and %VO_{2p} in female populations compared to males (21,22), the effect of CRP on all variables of CRF in women is still unknown.

METHODS

A quasi-experimental study was conducted, including patients diagnosed with chronic heart failure who underwent a cardiac rehabilitation program at Centro Médico Nacional "20 de Noviembre" from June 2019 to December 2023. Inclusion criteria were age over 18 years and a diagnosis of HF, both with reduced and preserved ejection fraction, according to American and European guidelines. Patients who did not complete the cardiac rehabilitation program or were in a decompensated state, had significant left ventricular outflow tract obstruction, acute infectious clinical states, and those without determination of cardiorespiratory variables for functional capacity assessment were excluded.

Program of Cardiac Rehabilitation

The outpatient phase II of the CRP included supervised physical training, nutritional and psychological assessment, and educational sessions on disease and cardiovascular risk factors. CPET was conducted at program entry and completion, using ramp protocols. The criteria for maximal effort during CPET were achieving $\geq 85\%$ of the expected maximal heart rate and a respiratory exchange ratio (RER) ≥ 1.15 .

Supervised concurrent training sessions were scheduled for 4 to 6 weeks, with 3 sessions per week, each lasting 60 minutes. Aerobic resistance training sessions included a 5-minute warm-up, a 20-minute main phase at 65-80% of HRR, and a 5-minute cooldown. For strength training, intensity was set at 30-50% of 1RM, with 5-minute warm-up and cooldown periods, in addition to physical qualities enhancement. Patients were instructed for virtual risk management sessions, exercise techniques, adherence strategies, psychosocial support, and received individual sessions on nutrition and respiratory retraining.

The primary outcome was the gains in cardiorespiratory variables obtained through CPET at the end of the program, including workload (expressed in METs), VO_{2peak}, %VO_{2p}, VE/VCO₂ slope, PO₂, CPO, and ventilatory thresholds: VT1, aerobic-anaerobic threshold (VAT), and second ventilatory threshold (VT2). Improvement in HRQoL after CRP was assessed using the SF-36 questionnaire. The secondary objective evaluated gains in patients based on left ventricular ejection fraction (EF), both with preserved ($\geq 50\%$) and reduced ($< 50\%$) EF.

Statistical Analyses

Continuous variables were expressed as means and standard deviations, and categorical variables were expressed in absolute values and percentages. Mann-Whitney test and chi-square test were used for comparative evaluation of continuous and non-paired data, respectively. Normality of distribution was assessed using the Kolmogorov-Smirnov test, considering $p < 0.05$ as statistically significant. All analyses were performed using SPSS Statistics version 27

Optimization of Cardiorespiratory Fitness and Quality of Life in Women with Chronic Heart Failure after a Cardiac Rehabilitation Program

(IBM) and Prism version 9.0 for Windows (GraphPad Software).

RESULTS

A total of 217 patients were included in the study, of which 65 (29.9%) were women. Significant differences were found in weight and height, both of which were higher in men. Additionally, tobacco consumption was more frequent in

men. Regarding cardiovascular history, men entering the CRP more frequently presented with chronic coronary syndrome. The average ventricular function was below 50% in both groups, and it was higher in women than in men (49.4% vs. 43.6%). For pharmacological treatment, men significantly had higher use of beta-blockers, statins, and antiplatelets compared to women. Patient characteristics are reported in Table 1.

Table 1. Study population characterization

	Women n= 65 (29.9%)	Men n=152 (70.0%)	p value
Age (years)	60.4	60.1	0.88
Weight (kg)	64.8	77.8	<0.001
High (m)	1.55	1.67	<0.001
Cardiovascular risk factors			
Obesity	13 (20%)	45 (29%)	0.11
Tobacco	15 (23%)	70 (46%)	<0.001
Tipo 2 diabetes	25 (38%)	65 (42%)	0.53
Arterial Hypertension	35 (53%)	103 (74%)	0.051
Dyslipidemia	23 (35%)	71 (46%)	0.11
Cardiovascular history			
CCS	26 (40%)	117 (76%)	<0.001
Valvulopathy	23 (35%)	42 (27%)	0.27
TAVR	7 (10.7%)	10 (6.5%)	0.33
TEEMVR	4 (6.1%)	3 (2%)	0.19
PAD	3 (4.6%)	12 (7%)	0.33
Dilated cardiomyopathy	7 (10.7%)	24 (15%)	0.30
Ventricular function			
LVEF	49.4%	43.6%	0.017
≥50%	38 (58.5%)	48 (31.5%)	
<50%	27 (41.5%)	104 (68.4%)	
Treatment			
ACEi	15 (23%)	47 (30%)	0.22
ARB	23 (35%)	65 (42%)	0.30
ARNI	10 (15%)	27 (17%)	0.66
Beta-blocker	42 (64%)	127 (83%)	0.005
Spironolactone	12 (18%)	31 (20%)	0.74
SGLT2 Inhibitor	10 (15%)	36 (23%)	0.56
Antiplatelets	32 (49%)	110 (72%)	0.001
Statin	42 (64%)	142 (93%)	<0.001
CCB	10 (15%)	25 (16%)	0.84
Diuretic	25 (38%)	57 (37%)	0.89

Abbreviations: ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin II receptor blockers; ARNI: neprilisin inhibitors; CCB=calcium-channel blockers; CCS=chronic coronary syndrome; LVEF= left ventricle ejection fraction; PAD=peripheral artery disease; TEEMVR= transcatheter edge-to-edge mitral valve repair; TAVR=transcatheter aortic valve replacement.

The training volume in women was 443.5 ± 170.6 METs-min/week and 470 ± 238.6 kcal/week, which was lower than in the male population with 513 ± 171.2 METs-min/week and

664.1 ± 239.2 kcal/week (Table 2). Attendance at CRP was 87.5% in both groups.

Optimization of Cardiorespiratory Fitness and Quality of Life in Women with Chronic Heart Failure after a Cardiac Rehabilitation Program

Table 2. Comparison between men and women of cardiorespiratory variables and quality of life at the beginning and end of the cardiac rehabilitation program.

Men				Women			
		Δ	p value			Δ	p value
Attendance	87.50%			87.50%			
Training volumen							
METs-min/week	513 ± 171.2			443.5 ± 170.6			
kcal/week	644.1 ± 239.3			470 ± 238.6			
Cardiorespiratory variables							
	INICIAL	FINAL			INICIAL	FINAL	
Workload (METs)	6.62 ± 2.53	10.34 ± 2.71	3.73	<0.001	5.40 ± 2.57	8.43 ± 2.59	3.02 <0.001
VO ₂ peak METs	5.39 ± 1.98	6.98 ± 2.49	1.59	<0.001	4.46 ± 1.53	6.29 ± 2.27	1.83 <0.001
%VO ₂ p	67.83 ± 24.89	87.5 ± 30.97	19.75	<0.001	56.62 ± 20.11	80.12 ± 30.32	23.50 <0.001
VE/VCO ₂ slope	38.53 ± 7.12	40.51 ± 26.00	2.23	0.367	39.58 ± 9.39	39.07 ± 0.77	-0.51 0.736
PO ₂ (ml/kg/min)/bpm	11.77 ± 3.50	13.69 ± 3.15	1.93	<0.001	8.19 ± 3.29	9.40 ± 2.65	1.21 0.021
TRCVO ₂ (s)	173.73 ± 65.90	149.39 ± 44.64	-24.35	<0.001	177.04 ± 68.28	161.67 ± 55.77	-15.36 0.162
CPO	8322.64 ± 3736.52	10466.52 ± 4662.02	2143.88	<0.001	8374.15 ± 3479.13	10291.26 ± 4052.31	1917.10 0.004
VT1 (METs)	2.92 ± 1.16	3.33 ± 1.10	0.42	0.002	2.55 ± 1.19	3.00 ± 0.96	0.44 0.020
VAT (METs)	3.86 ± 1.70	4.94 ± 1.76	1.08	<0.001	3.37 ± 1.96	4.59 ± 1.69	1.22 <0.001
VT2 (METs)	4.09 ± 2.45	6.03 ± 2.39	1.96	<0.001	2.84 ± 2.65	4.98 ± 2.35	2.14 <0.001
HRQoL (%)							
	69.38 ± 18.37	80.93 ± 12.94	11.55	<0.001	62.03 ± 18.37	78.81 ± 12.90	16.77 <0.001

Abbreviations: VO₂peak=peak oxygen consumption, %VO₂p=% of predicted VO₂, PO₂= oxygen pulse, CPO= cardiac power output, HRQoL= health-related quality of life; TRCVO₂= time to recovery of VO₂ kinetics, VT1= first ventilatory threshold, VAT= aerobic-anaerobic threshold VT2= second ventilatory threshold.

Exercise capacity at the time of entry to CRP was lower in women (workload: 5.4±2.57 METs and VO₂peak: 4.46±1.53 METs) than in men (workload: 6.62±2.53 METs and VO₂max: 5.39±1.98 METs). Except for the VE/VCO₂ slope and TRCVO₂, significant gains were obtained in all cardiorespiratory variables (workload, VO₂peak, %VO₂p, PO₂, CPO, and ventilatory thresholds) in women after CRP. In men, significant gains were not observed only in the

VE/VCO₂ slope. HRQoL significantly improved in both groups (Table 2).

When assessing patients with EF <50%, in women, the CRF variables that did not show significant improvement were the VE/VCO₂ slope, TRCVO₂, and CPO. For men, significant improvement was maintained in all CRF variables, except for the VE/VCO₂ slope. Significant improvement in the quality of life was maintained in this subgroup, regardless of gender (Table 3).

Table 3. Comparison between men and women with EF <50% of cardiorespiratory variables and quality of life at the beginning and end of the cardiac rehabilitation program.

Men				Women			
		Δ	p value			Δ	p value
Attendance	87.22%			88.58%			
Training volumen							
METs-min/week	515.82 ± 178.26			437.55 ± 164.54			
kcal/week	658.51 ± 251.93			454.74 ± 138.70			

Optimization of Cardiorespiratory Fitness and Quality of Life in Women with Chronic Heart Failure after a Cardiac Rehabilitation Program

Cardiorespiratory variables								
	INICIAL	FINAL			INICIAL	FINAL		
Workload (METs)	6.34 ± 2.45	10.23 ± 2.65	3.89	<0.001	4.95 ± 2.21	7.99 ± 2.63	3.04	<0.001
VO ₂ máx (METs)	5.22 ± 2.03	6.87 ± 2.63	1.65	<0.001	4.30 ± 1.70	6.15 ± 2.51	1.85	0.003
%VO ₂ p	63.88 ± 24.83	83.62 ± 31.25	19.75	<0.001	53.87 ± 17.96	77.90 ± 29.99	24.03	0.001
VE/VCO ₂ slope	39.13 ± 7.86	41.64 ± 31.12	2.89	0.427	38.69 ± 6.38	38.85 ± 3.67	0.17	0.907
PO ₂ (ml/min)/bpm	11.83 ± 3.72	13.56 ± 4.41	1.73	0.003	7.98 ± 2.27	9.39 ± 1.54	1.41	0.011
TRCVO ₂ (s)	183.69 ± 71.89	151.30 ± 48.40	-32.39	<0.001	173.59 ± 47.75	174.33 ± 52.40	-0.74	0.957
CPO	7635.90 ± 3550.93	9942.55 ± 4715.75	2306.65	<0.001	7884.51 ± 3216.51	8843.74 ± 3284.85	959.2	0.283
VT1 (METs)	2.76 ± 1.19	3.35 ± 1.12	0.62	<0.001	2.10 ± 1.39	3.051 ± 1.02	0.95	0.006
VAT (METs)	3.79 ± 1.78	4.90 ± 1.78	1.11	<0.001	3.02 ± 2.29	4.54 ± 1.61	1.52	0.007
VT2 (METs)	4.22 ± 2.46	6.04 ± 2.44	1.87	<0.001	2.54 ± 2.78	5.16 ± 2.24	2.62	<0.001
HRQoL (%)	68.31 ± 18.20	80.56 ± 13.13	12.25	<0.001	63.66 ± 16.51	78.33 ± 13.86	14.67	0.001

Abbreviations: VO₂peak=peak oxygen consumption, %VO₂p=% of predicted VO₂, PO₂= oxygen pulse, CPO= cardiac power output, HRQoL= health-related quality of life; TRCVO₂= time to recovery of VO₂ kinetics, VT1= first ventilatory threshold, VAT= aerobic-anaerobic threshold VT2= second ventilatory threshold.

In patients with EF ≥50%, the CRF variables that did not improve in men were the VE/VCO₂ slope, TRCVO₂, and VT1. In the case of women, there was no significant

improvement in PO₂, TRCVO₂, and VT1. In both cases, HRQoL improved significantly, but women did not reach the predicted improvement in HRQoL (Table 4).

Table 4. Comparison between men and women with EF ≥50% of cardiorespiratory variables and quality of life at the beginning and end of the cardiac rehabilitation program.

	Men				Women			
			Δ	p value			Δ	p value
Attendance	88.31%				86.73%			
Training volume								
METs-min/week	506.54 ± 153.28				447.91 ± 151.62			
Kcal/week	611.70 ± 198.67				481.23 ± 161.20			
Cardiorespiratory variables								
	INICIAL	FINAL			INICIAL	FINAL		
Workload (METs)	7.22 ± 2.64	10.59 ± 2.85	3.37	<0.001	5.72 ± 2.79	8.74 ± 2.56	3.02	<0.001
VO ₂ máx (METs)	5.76 ± 1.84	7.22 ± 2.15	1.45	<0.001	4.57 ± 1.44	6.40 ± 2.12	1.82	<0.001
%VO ₂ p	76.41 ± 22.99	96.16 ± 28.85	19.7	<0.001	58.58 ± 21.54	81.70 ± 30.85	23.12	<0.001
VE/VCO ₂ slope	37.23 ± 5.40	38.05 ± 6.41	0.82	0.474	40.21 ± 11.09	39.22 ± 9.79	-0.99	0.695
PO ₂ (ml/min)/bpm	11.63 ± 3.01	13.99 ± 3.55	2.36	<0.001	8.33 ± 3.88	9.41 ± 3.24	1.08	0.173
TRCVO ₂ (s)	152.16 ± 43.94	145.25 ± 32.25	-6.92	0.401	179.50 ± 80.30	152.68 ± 57.01	-26.82	0.099
CPO	9810.58 ± 3730.69	11601.79 ± 4378.24	179	0.034	8722.05 ± 3656.20	11319.76 ± 4266.90	2597.	0.006
VT1 (METs)	3.27 ± 1.03	3.28 ± 1.06	0.01	0.810	2.88 ± 0.91	2.97 ± 0.93	0.09	0.504
VAT (METs)	4.00 ± 1.53	5.02 ± 1.73	1.02	0.002	3.61 ± 1.68	4.62 ± 1.76	1.01	0.009

Optimization of Cardiorespiratory Fitness and Quality of Life in Women with Chronic Heart Failure after a Cardiac Rehabilitation Program

VT2 (METs)	3.83 ± 2.44	5.99 ± 2.32	2.17	<0.001	3.05 ± 2.57	4.85 ± 2.44	1.80	0.002
QRQoL (%)	71.70 ± 18.72	81.73 ± 12.50	10.03	0.003	60.87 ± 16.68	79.14 ± 13.24	18.27	<0.001

Abbreviations: VO₂peak=peak oxygen consumption, %VO₂p=% of predicted VO₂, PO₂= oxygen pulse, CPO= cardiac power output, HRQoL= health-related quality of life; TRCVO₂= time to recovery of VO₂ kinetics, VT1= first ventilatory threshold, VAT= aerobic-anaerobic threshold VT2= second ventilatory threshold.

DISCUSSION

In this study of patients with HF who completed a CRP, gains in CRF and HRQoL variables were obtained in both women and men. Consistent with the literature, women had lower tobacco consumption, lower ischemic etiology (40% vs. 76%), and better left ventricular function. Regarding treatment, they had lower use of beta-blockers, statins, and antiplatelets compared to men.

In a previous study, Matos et al assessed the effects of CRP by gender in patients with ischemic HF (21). Their proportion of included women was 19%, with better initial exercise tolerance and higher ventricular function. They assessed improvement in exercise capacity only with VO₂peak and %VO₂p. Their absolute gains in these parameters were lower than those obtained in our study, despite conducting a more prolonged CRP; possibly due to the training volume quantified in our center, where 90 minutes of weekly aerobic resistance is monitored at sufficient intensity to generate gains. Other CRF variables and changes in HRQoL were not assessed. In our study, attendance in the program for women was 87.5%, which did not differ from men, contrary to what was described in previous reviews.

For the primary outcome, despite implementing a CRP with less duration than recommended, and women presenting lower exercise capacity during the initial CPET, as well as lower training volume, significant improvement in exercise capacity was achieved at the end of the program (workload 8.43±2.59 METs, VO₂peak 6.29±2.27 METs), although lower than that obtained in men (workload 10.34 ± 2.71 METs, VO₂peak 6.98 ± 2.49 METs), it was sufficient for women to optimize %VO₂p (56.62%±20.11 vs 80.12%±30.32), implying improvement in clinical outcomes. Similar gains were made in PO₂, CPO, and ventilatory threshold displacements. The VE/VCO₂ slope, an indicator of ventilatory efficiency, did not improve in any case, as expected due to the short duration of the intervention and the level of ventilatory inefficiency reached at the end of the program when pushed to even higher intensity. This trend persisted regardless of ventricular function.

Typically, in patients with HF, some may not show complete ventilatory thresholds due to a combination of energy systems or the predominance of the glycolytic system over the oxidative. Regarding ventilatory thresholds, in our cohort at the start of the program, not all patients reached the zone of metabolic instability during the initial CPET, so the initial

average values of VT2 were lower than the VAT. Afterward, however, the appearance of VT2 was observed in those patients who did not initially present it, and in all cases, ventilatory thresholds shifted, demonstrating greater tolerance to metabolic instability and improvement in oxidative capacity and buffering systems, ultimately resulting in greater tolerance to submaximal efforts.

Despite gains in CRF in all patients, the results observed in the population with EF <50% did not optimize %VO₂p in women at the end of CRP (77.9% ± 29.99). Also, there was no significant improvement in TRCVO₂ and CPO. In men, the results were consistent with the general population. In the EF ≥50% subgroup, women improved exercise tolerance, reaching a %VO₂p >80%. However, they did not show improvement in PO₂, TRCVO₂, and VT1. In men, TRCVO₂ and VT1 were the CRF variables that did not show improvement after CRP, possibly due to alterations in ventricular filling in women with HF with preserved ejection fraction.

Despite the multiple existing barriers to entry, adherence, and completion of CRP in women(21,22), we achieved an attendance >80%. It is noteworthy that the results obtained in the primary outcome in women were achieved despite women not reaching the minimum training volume recommended by clinical guidelines (23). Thus, they showed significant improvement in exercise tolerance assessed by workload and VO₂peak, %VO₂p, PO₂, CPO, and ventilatory threshold displacements. This may imply that if the recommended minimum training volume is achieved, it could significantly improve the cardiorespiratory variables that did not show significant gains in women, as well as achieve a score >80% in quality of life. We assume that the differences in training volume between groups were due to lower intensity in women, as the duration and frequency were the same in both cases; so it would be worth exploring results with a higher intensity, frequency of sessions or program duration to achieve sufficient training volume to maximize gains in the female population.

Results varied according to ventricular function, maintaining significant improvements in exercise tolerance in all cases, without reaching a %VO₂p >80% in women with EF <50%. Additionally, it is important to note that patients undergoing structural interventional procedures, such as transcatheter aortic valve implantation and edge-to-edge repair of the mitral valve, were included. In these patients, the intervention

Optimization of Cardiorespiratory Fitness and Quality of Life in Women with Chronic Heart Failure after a Cardiac Rehabilitation Program

was safe, with no device-related complications during CPET or training sessions.

HRQoL, assessed by the SF-36 questionnaire, was lower in women at the beginning of the program. Despite this, and despite showing greater deltas (absolute gains) compared to men, the predicted HRQoL at the end of CRP was lower for women.

Our study has several limitations. Firstly, it was conducted at a single center, and a small number of participants were included. Changes in ventricular function at the end of CRP were not assessed as part of the adaptations to physical training. Like previous studies, the proportion of included women was low, at 29.9% (21,22).

To our knowledge, this is the first study evaluating the effects of a CRP on patients with HF based on gender and ventricular function, assessing CRF with all cardiorespiratory variables obtained through CPET and HRQoL. Significant gains were found in all cardiorespiratory variables studied from CPET, except for the VE/VCO₂ slope. This supports the need to implement measures to ensure women's entry into and completion of CRP; because, although gains in CRF are lower compared to men, they are possibly sufficient to improve outcomes, including increased survival and a lower rate of long-term hospitalizations (24–26).

CONCLUSION

In female patients with HF, the implementation of a CRP leads to significant gains in all cardiorespiratory variables, achieving optimization of the %VO_{2p} like the male population. The exception to this improvement was the VE/VCO₂ slope, which did not improve in any case, regardless of ventricular function. The improvement in HRQoL is greater in women, although it persists below target levels. Therefore, efforts should be directed towards measures that ensure the enrollment, adherence, and completion of CRP in the female population.

REFERENCES

- I. Urbich M, Globe G, Pantiri K, Heisen M, Bennison C, Wirtz HS, et al. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014–2020). *Pharmacoeconomics*. 2020;38(11):1219–36.
- II. Wills WB, Athilingam P, Beckie TM. Exercise-Based Cardiac Rehabilitation in Women with Heart Failure: A Review of Enrollment, Adherence, and Outcomes. *Heart Fail Rev*. 2023;28(6):1251–66.
- III. Tsao CW, Aday AW, Almarazooq ZI, Anderson CAM, Arora P, Avery CL, et al. Heart Disease and Stroke Statistics—2023 Update: A Report From the American Heart Association. *Circulation*. 2023;147(8):e93–621.
- IV. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure Developed by the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology (ESC) With the Special Contribution of the Heart Failure Association (HFA) of the ESC. *Eur Hear J*. 2021;42(36):ehab368.
- V. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2022;79(17):1757–80.
- VI. Khan SS, Beach LB, Yancy CW. Sex-Based Differences in Heart Failure JACC Focus Seminar 7/7. *J Am Coll Cardiol*. 2022;79(15):1530–41.
- VII. Dewan P, Rørth R, Jhund PS, Shen L, Raparelli V, Petrie MC, et al. Differential Impact of Heart Failure With Reduced Ejection Fraction on Men and Women. *J Am Coll Cardiol*. 2019;73(1):29–40.
- VIII. Schorr M, Dichtel LE, Gerweck AV, Valera RD, Torriani M, Miller KK, et al. Sex Differences in Body Composition and Association with Cardiometabolic Risk. *Biol Sex Differ*. 2018;9(1):28.
- IX. Karastergiou K, Smith SR, Greenberg AS, Fried SK. Sex Differences in Human Adipose Tissues – The Biology of Pear Shape. *Biol Sex Differ*. 2012;3(1):13.
- X. Leiro MGC, Martín MJ. Insuficiencia Cardíaca. ¿Son Diferentes las Mujeres? *Rev Española Cardiol*. 2006;59(7):725–35.
- XI. Taylor RS, Dalal HM, Zwisler AD. Cardiac Rehabilitation for Heart Failure: ‘Cinderella’ or evidence-based pillar of care? *Eur Hear J*. 2023;44(17):1511–8.
- XII. Piepoli MF, Davos C, Francis DP, Coats AJS, Collaborative E. Exercise Training Meta-analysis of Trials in Patients with Chronic Heart Failure (ExTraMATCH). *BMJ*. 2004;328(7433):189.
- XIII. O’Connor CM, Whellan DJ, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ, et al. Efficacy and Safety of Exercise Training in Patients With Chronic Heart Failure: HF-ACTION Randomized Controlled Trial. *JAMA*. 2009;301(14):1439–50.
- XIV. Taylor RS, Walker S, Smart NA, Piepoli MF, Warren FC, Ciani O, et al. Impact of Exercise-Based Cardiac Rehabilitation in Patients with Heart Failure (ExTraMATCH II) on Mortality and Hospitalisation: An Individual Patient Data Meta-analysis of Randomised Trials. *Eur J Hear Fail*. 2018;20(12):1735–43.

Optimization of Cardiorespiratory Fitness and Quality of Life in Women with Chronic Heart Failure after a Cardiac Rehabilitation Program

- XV. Bjarnason-Wehrens B, Nebel R, Jensen K, Hackbusch M, Grilli M, Gielen S, et al. Exercise-Based Cardiac Rehabilitation in Patients With Reduced Left Ventricular Ejection Fraction: The Cardiac Rehabilitation Outcome Study in Heart Failure (CROS-HF): A systematic review and meta-analysis. *Eur J Prev Cardiol.* 2019;27(9):929–52.
- XVI. Turk-Adawi K, Supervia M, Lopez-Jimenez F, Adawi A, Sadeghi M, Grace SL. Women-Only Cardiac Rehabilitation Delivery Around the World. *Hear, Lung Circ.* 2021;30(1):135–43.
- XVII. Khadanga S, Gaalema DE, Savage P, Ades PA. Underutilization of Cardiac Rehabilitation in Women. *J Cardiopulm Rehabilitation Prev.* 2021;41(4):207–13.
- XVIII. Supervía M, Medina-Inojosa JR, Yeung C, Lopez-Jimenez F, Squires RW, Pérez-Terzic CM, et al. Cardiac Rehabilitation for Women: A Systematic Review of Barriers and Solutions. *Mayo Clin Proc.* 2017;92(4):565–77.
- XIX. Galati A, Piccoli M, Tourkmani N, Sgorbini L, Rossetti A, Cugusi L, et al. Cardiac Rehabilitation in Women. *J Cardiovasc Med.* 2018;19(12):689–97.
- XX. Ghisi GL de M, Kin SM R, Price J, Beckie TM, Mamataz T, Naheed A, et al. Women-Focused Cardiovascular Rehabilitation: An International Council of Cardiovascular Prevention and Rehabilitation Clinical Practice Guideline *. *Can J Cardiol.* 2022;38(12):1786–98.
- XXI. Vilela EM, Ladeiras-Lopes R, Joao A, Braga J, Torres S, Ribeiro J, et al. Differential Impact of a Cardiac Rehabilitation Program in Functional Parameters According to Patient Gender. *Am J Cardiovasc Dis.* 2020;10(4):367–75.
- XXII. Szmigielska K, Jegier A. Clinical Outcomes of Cardiac Rehabilitation in Women with Coronary Artery Disease—Differences in Comparison with Men. *J Pers Med.* 2022;12(4):600.
- XXIII. Pelliccia A, Gati S, Bäck M, Börjesson M, Caselli S, et al. 2020 ESC Guidelines on Sports Cardiology and Exercise in Patients with Cardiovascular Disease: The Task Force on Sports Cardiology and Exercise in Patients with Cardiovascular Disease of the European Society of Cardiology (ESC). *Eur Hear J.* 2020;42(1):17–96.
- XXIV. Scharf C, Merz T, Kiowski W, Oechslin E, Schalcher C, Rocca HPBL. Noninvasive Assessment of Cardiac Pumping Capacity During Exercise Predicts Prognosis in Patients with Congestive Heart Failure. *Chest.* 2002;122(4):1333–9.
- XXV. Corrà U, Mezzani A, Bosimini E, Scapellato F, Imparato A, Giannuzzi P. Ventilatory Response to Exercise Improves Risk Stratification in Patients with Chronic Heart Failure and Intermediate Functional Capacity. *Am Hear J.* 2002;143(3):418–26.
- XXVI. Scrutinio D, Passantino A, Lagioia R, Napoli F, Ricci A, Rizzon P. Percent Achieved of Predicted Peak Exercise Oxygen Uptake and Kinetics of Recovery of Oxygen Uptake after Exercise for Risk Stratification in Chronic Heart Failure. *Int J Cardiol.* 1998;64(2):117–24.