Case Series

# Cardiac Rehabilitation Improves Cardiometabolic Health

in Young Patients with Nonischemic Dilated Cardiomyopathy

Samuel G. Wittekind, MD Yvette Gerdes, MS Wayne Mays, MS Clifford Chin, MD John L. Jefferies, MD, MPH Nonischemic dilated cardiomyopathy is deadly and costly, and treatment options are limited. Cardiac rehabilitation has proved safe and beneficial for adults with various types of heart failure. Therefore, we retrospectively evaluated the hypothesis that rehabilitation is safe and improves cardiometabolic health in young patients with nonischemic dilated cardiomypathy.

From 2011 through 2015, 8 patients (4 males) (mean age,  $20.6 \pm 6.6$  yr; range, 10-31 yr) underwent rehabilitation at our institution. They were in American Heart Association class C or D heart failure and were on maximal medical therapy. Their mean left ventricular ejection fraction at baseline was  $0.26 \pm 0.15$ . Two patients had a left ventricular assist device, and 2 were inpatients. To evaluate safety, we documented adverse events during rehabilitation sessions. Clinical endpoints were measured at baseline, immediately after completing rehabilitation, and after one year.

Patients attended 120 of 141 possible sessions (85%), with no adverse events. There were no marked changes in mean left ventricular ejection fraction or body mass index. The patients' mean waist circumference decreased by 1.37  $\pm$  0.6 in (n=5; 95% Cl, -2.1 to -0.63). Their 6-minute walk distance increased by a mean of 111  $\pm$  75 m (n=5; 95% Cl, 18–205).

In our small sample of young patients with nonischemic dilated cardiomyopathy, cardiac rehabilitation was feasible and was associated with minimal risk. Our findings suggest that prospective studies in this population are warranted. (Tex Heart Inst J 2018;45(1):27-30)

**Key words:** Cardiomyopathy, dilated/physiopathology/therapy; exercise therapy; heart failure/rehabilitation; quality of life; retrospective studies; severity of illness index; walking/physiology; young adult

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© 2018 by the Texas Heart® Institute, Houston eart failure (HF) from nonischemic dilated cardiomyopathy (DCM) is the most frequent diagnosis in pediatric patients referred for heart transplantation, and an increasing number of them are being treated with left ventricular assist devices (LVAD) as a bridge to transplantation.¹ Functional capacity, evaluated by means of exercise testing, is a strong predictor of cardiac events,² and it can be substantially impaired by central obesity, which is common in HF. Therefore, targeted weight-loss strategies are recommended in this population.³ Cardiac rehabilitation (CR) is an effective and safe treatment for adults with HF, but to our knowledge, no data have been published regarding the safety and early benefits of CR in young patients with nonischemic DCM. We evaluated the hypothesis that CR is safe and associated with improved cardiometabolic health in this population.

# **Patients and Methods**

This retrospective study was approved by our institutional review board. We searched the database of the Cardiac Rehabilitation Program at Cincinnati Children's Hospital Medical Center for patients with nonischemic DCM who were referred between 2011 and 2015. The diagnosis was independently confirmed by 2 cardiologists. For each patient, we recorded baseline characteristics, including demographic information, body mass index (BMI), waist circumference, medications, American Heart Association (AHA) HF class, quality of life (QOL) score (as measured by the Pediatric Quality of Life Inventory [PedsQL] scoring tool),<sup>4</sup> echocardiographic left ventricular ejection fraction (LVEF), serum brain natriuretic peptide (BNP) level, cardiopulmonary exercise test (CPET) results, and 6-minute walk distance test (6MWD).

TABLE I. Patients' Baseline Demographic and Clinical Characteristics

Pt. No.	Age (yr), Sex	DCM Cause	Medications	VAD	ICD	AHA Class	PedsQL Score	Weight (kg)	<b>BMI</b> (kg/m²)	WC (in)	6MWD (m)	LVEF	BNP (pg/mL)
1	14, M	Idiopathic	Amiodarone, aspirin, lisinopril, and spironolactone	No	No	С	91	51	16.5	_	_	0.23	760
2	31, F	Peripartal	Lisinopril	No	No	С	_	95	36.7	42.3	365	0.56	32
3	25, M	Idiopathic	Aspirin, carvedilol, lisinopril, sildenafil, and warfarin	Yes	No	D	_	121	38.8	_	_	0.15	394
4	17, F	Idiopathic	Carvedilol, furosemide, and lisinopril	No	No	С	54	162	59.3	58.5	345	0.28	169
5	20, F	Idiopathic	Aspirin, carvedilol, furosemide, lisinopril, and spironolactone	No	No	D	_	102	39.3	_	447	0.18	345
6	20, F	Idiopathic	Aspirin, carvedilol, furosemide, lisinopril, and spironolactone	No	Yes	С	61	107	41.2	49.2	480	0.15	123
7	10, M	Idiopathic	Enalapril, furosemide, spironolactone, and warfarin	Yes	No	D	_	103	45.6	45.8	180	0.15	339
8	28, M	Anthra- cycline- induced	Atorvastatin, carvedilol, chlorothiazide, clonidine, enalapril, and warfarin	No	No	С	47	63	28.2	38.2	444	0.39	237

6MWD = 6-minute walk distance; AHA = American Heart Association heart failure class; BMI = body mass index; BNP = brain natriuretic peptide; DCM = dilated cardiomyopathy; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; PedsQL = Pediatric Quality of Life Inventory; Pt. = patient; VAD = ventricular assist device; WC = waist circumference

Eight patients whose primary cardiologists had prescribed CR for the indication of HF with reduced LVEF were included in the study (Table I). Their mean age was  $20.6 \pm 6.6$  years (range, 10-31 yr), and 4 were male. The group was predominately obese (mean BMI, 38.2)  $\pm$  12.5 kg/m<sup>2</sup>; mean waist circumference, 46.8  $\pm$  7.7 in). Six patients had idiopathic DCM, one had anthracycline-induced cardiomyopathy, and one had peripartum cardiomyopathy. According to the AHA's objectives for assessment of HF, 5 patients were in class C, and 3, in class D. The mean baseline LVEF was  $0.26 \pm 0.15$ , and the mean baseline indexed maximum oxygen consumption was  $17 \pm 5$  mL/kg/min (data not shown). All patients had been prescribed maximal medical therapy at the time of CR. Two patients participated in CR as inpatients, and 2 were on LVAD support.

The CR sessions consisted of supervised, personalized exercise therapy, administered in the hospital by a single exercise physiologist according to the standards of the American Association of Cardiovascular and Pulmonary Rehabilitation. Each session lasted at least 45 minutes and included active warm-up, cardiovascular exercise, strength, flexibility, and cooldown components. The patient's heart rate reserve (HRR) was calculated from baseline CPET values, and 75% to 85% of HRR was maintained for at least half of each session. Patients were encouraged to attend 2 sessions per week for up to 16 weeks.

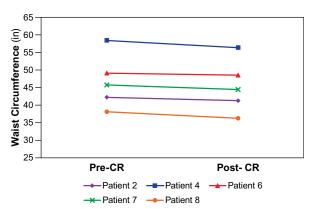
Immediately after completion of CR, endpoints were reevaluated. The echocardiograms nearest to the start and end of CR were compared. Safety was evaluated by counting adverse events during CR sessions. All-cause

and cardiovascular-related hospitalizations during a 12-month follow-up period were totaled.

Statistical analysis was conducted by using JMP® Pro 12 software (SAS Institute Inc.). Continuous demographic and clinical variables were summarized as mean  $\pm$  SD. Baseline and post-CR measurements of waist circumference and 6MWD were compared with use of a 2-tailed paired-sample t test. Statistical significance could not be evaluated because of the small number of patients.

## Results

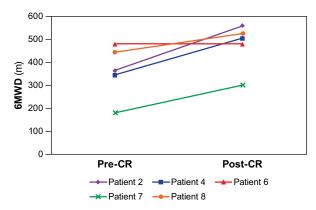
The patients attended 120 of 141 (85%) possible CR sessions. There were no deaths, adverse events necessitating discontinuation of CR sessions, or cardiovascular-related hospitalizations during patients' participation. In



**Fig. 1** Graph shows waist circumferences of 5 patients, before and after cardiac rehabilitation (CR). The mean circumference decreased by  $1.37 \pm 0.6$  in (95% CI, -2.1 to -0.63).

patients who had post-CR endpoints recorded (n=5), mean waist circumference decreased by  $1.37\pm0.6$  in (95% CI, -2.1 to -0.63) (Fig. 1); there was no significant change in BMI. The 6MWD increased by a mean of  $111\pm75$  m (n=5; 95% CI, 18–205) (Fig. 2). The mean serum BNP level decreased, and the QOL score improved in all patients in whom it was measured (Table II). There was no marked change in left ventricular systolic function after CR (mean LVEF, 0.28  $\pm$  0.17).

Within one year of starting CR, one patient with an LVAD underwent heart transplantation, and the other remained stable at home. One patient was hospitalized twice for HF exacerbations that necessitated medication adjustment, and another patient was hospitalized for stroke, possibly due to embolism of an undiagnosed left ventricular thrombus.



**Fig. 2** Graph shows 6-minute walk distances (6MWD) of 5 patients, before and after cardiac rehabilitation (CR). The mean distance increased by  $111 \pm 75$  m (95% Cl, 18-205).

TABLE II. Clinical Endpoints Immediately after Cardiac Rehabilitation and at One Year

			Imme	One Year									
Pt. No.	AHA Class	PedsQL Score	Sessions Attended (%)	Weight (kg)	<b>BMI</b> (kg/m²)	WC (in)	<b>6MWD</b> (m)	LVEF	BNP (pg/mL)	AHA Class	OHT, VAD, or Death	Total Hosp	CV Hosp
1	С	98	92	59	18.9	_	_	0.16	199	С	None	0	0
2	А	_	86	91	35	41.3	560	0.66	_	Α	None	0	0
3	D	_	100	119	38	_	_	0.15	_	D	None	0	0
4	С	61	100	159	58.2	56.5	505	0.30	70	С	None	0	0
5	С	_	100	108	41.7	_	_	0.17	222	С	None	3	2
6	С	67	67	107	41.4	48.6	480	0.26	84	С	None	1	1
7	D	_	100	100	44.4	44.4	300	0.20	216	А	OHT	3	0
8	С	60	66	60	27	36.3	525	0.34	_	С	None	1	1

6MWD = 6-minute walk distance; AHA = American Heart Association heart failure class; BMI = body mass index; BNP = brain natriuretic peptide; CV = cardiovascular; Hosp = hospitalizations; LVEF = left ventricular ejection fraction; OHT = orthotopic heart transplantation; PedsQL = Pediatric Quality of Life Inventory; Pt. = patient; VAD = ventricular assist device; WC = waist circumference

## **Discussion**

Diminished functional capacity, which is predictive of adverse cardiovascular outcomes such as death and the need for a heart transplant, can be worsened by obesity, a condition common in patients with HF.<sup>2,3</sup> Many children with HF also have a poor QOL, which is associated with depression and anxiety.4 Reducing obesity and improving QOL in young patients with HF and nonischemic DCM may help prevent decompensation or, at least, put patients with advanced HF in a better psychological state before heart transplantation or the implantation of a ventricular assist device. In our young patient population, functional capacity and QOL improved after exercise therapy, and this finding is consistent with that in O'Connor and colleagues' study of exercise training in adults with HF.5 We also observed an intriguing decrease in serum BNP levels in our patients; this may indicate that optimal management of HF leads to lower ventricular wall stress.

Limitations of this study include the small number of patients, which indicates the novelty of treating young HF patients with CR. Moreover, we did not control for medications, which may have had a confounding effect on our results. Although some patients participated in CR as inpatients and others as outpatients, only one exercise physiologist administered the sessions, which meant little or no variability in technique. Finally, because most patients did not have a post-therapy CPET available, our ability to state the effect of CR on functional capacity is limited; however, the magnitude of the increase in their 6MWD offers compelling evidence that CR was beneficial.

# Conclusion

Young patients with nonischemic DCM, including those with advanced HF that necessitates an LVAD, may be able to participate in supervised exercise therapy with minimal risk. In our patients with HF, we observed a reduction in central adiposity, improved 6MWD, a decrease in serum BNP, and improved patient-reported QOL after exercise therapy—results that are similar to those in older adults with HF. A more robust, prospective study of the safety and effects of CR in young patients with nonischemic DCM is needed to confirm these findings and to examine clinical outcomes in more depth.

## References

- 1. Jefferies JL, Towbin JA. Dilated cardiomyopathy. Lancet 2010;375(9716):752-62.
- Rostagno C, Olivo G, Comeglio M, Boddi V, Banchelli M, Galanti G, Gensini GF. Prognostic value of 6-minute walk corridor test in patients with mild to moderate heart failure: comparison with other methods of functional evaluation. Eur J Heart Fail 2003;5(3):247-52.
- 3. Shrier I. The "obesity paradox" is not a paradox: time to focus on effective treatments. JACC Heart Fail 2016;4(3):234.
- Wilmot I, Cephus CE, Cassedy A, Kudel I, Marino BS, Jefferies JL. Health-related quality of life in children with heart failure as perceived by children and parents. Cardiol Young 2016;26(5):885-93.
- 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.