Heart Failure EF: Exercise and its Cardiovascular Effects 2023

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Disclosures

Speakers Bureau – Actelion Pharmaceuticals, J&J, BI, Astra Zeneca, Pfizer and BMS

Heart Failure Terminology

- **Heart failure** is a global term for the **physiological state** in which cardiac output is insufficient for the body's needs. Heart Failure is a condition in which a problem with the structure or function of the heart impairs its ability to supply sufficient blood flow to meet the body's needs.

Heart Failure Pathophysiology

Heart failure is caused by any condition which reduces the efficiency of the myocardium leading to overload on the myocardium. Over time the increased workload will produce changes to the heart:

- Reduced contractility, or force of contraction, due to overloading of the ventricle.
- A reduced stroke volume, as a result of a failure of systole, diastole or both.
- Increased heart rate, stimulated by increased sympathetic activity in order to maintain cardiac output.
- Hypertrophy of the myocardium, caused by the terminally differentiated heart muscle fibers increasing in size in an attempt to improve contractility.
- Enlargement of the ventricles, contributing to the enlargement and spherical shape of the failing heart.

Heart Failure Statistics

Prevalence

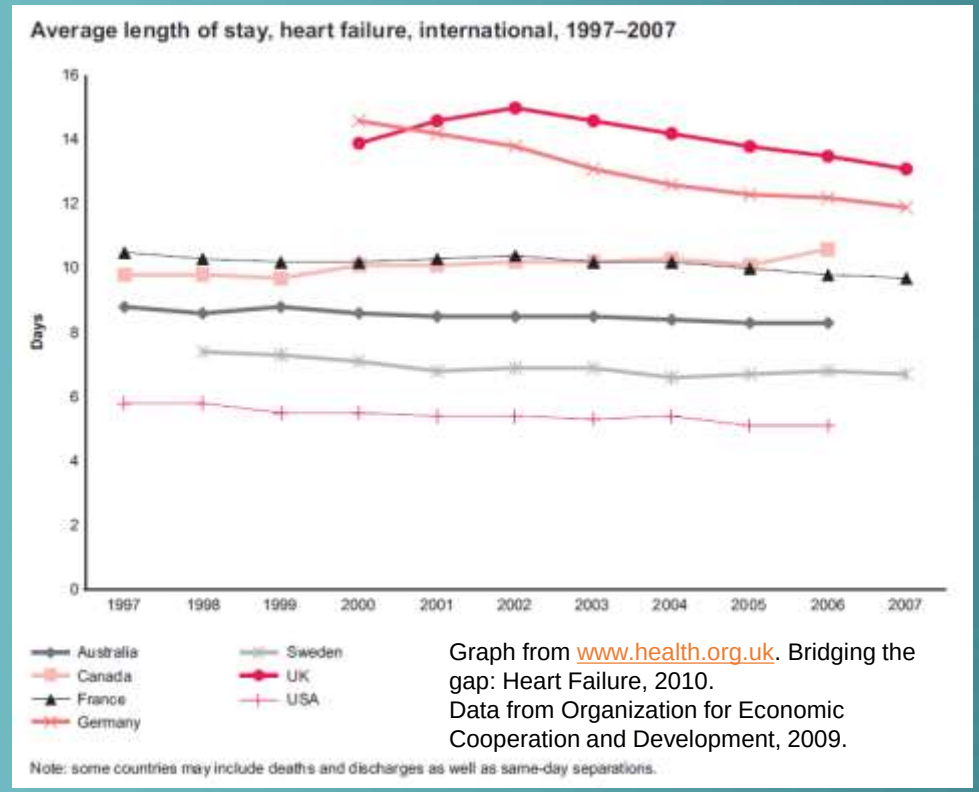
- Heart failure (HF) affects an estimated 5.1 million Americans ≥ 20 years of age.
- 400,000 new cases of heart failure are diagnosed in the United States annually.

Incidence

- One-percent of adults 50 to 60 years of age.
- Ten-percent of adults 80 years of age or older.

Heart Failure Is Associated with High Hospitalization and Readmission Rates

- In 2010, there were 1 million hospitalizations in the US with HF as the principal diagnosis[1]
  - Hospitalization rate did not change significantly from 2000[1]
- Average length of hospital stay
  - Approximately 5 days (US)[2]
  - 11 days (Europe)[3]
- HF is also associated with high readmission rates:
  - ~25% all-cause readmission within 30 days and ~50% within 6 months[5]



Graph from www.health.org.uk. Bridging the gap: Heart Failure, 2010.
Data from Organization for Economic Cooperation and Development, 2009.

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1. CDC NCHS National Hospital Discharge Survey, 2000-2010
2. Yancy et al. JACC, 2006.
3. Cleland et al. EuroHeart, 2003.
4. Krumholz HM, et al. Circ Cardiovas Qual Outcomes 2009.
5. Wexler DJ, et al. Am Heart J 2001.

Types of Heart Failure

Classification of heart failure is based on which heart function or which side of the heart is most affected by the condition.

- ***Systolic heart failure (HFrEF)*** – failure of contraction to pump blood out of the chambers. This is measured by ejection fraction (EF) or the percentage of blood that is ejected out of the ventricle. Normal is 50% or higher.
- ***Diastolic heart failure (HFpEF)*** – failure of relaxation to fill the chambers with blood
- ***Heart failure with mid-range EF (HFmEF)*** – EF 40-49%

NYHA Functional Classification

Class	Description
I (Mild)	No limitation of physical activity - ordinary physical activity doesn't cause tiredness, heart palpitations, or shortness of breath
II (Mild)	Slight limitation of physical activity, comfortable at rest, but ordinary physical activity results in tiredness, heart palpitations, or shortness of breath
III (Moderate)	Marked or noticeable limitations of physical activity, comfortable at rest, but less than ordinary physical activity causes tiredness, heart palpitations, or shortness of breath
IV (Severe)	Severe limitation of physical activity, unable to carry out any physical activity without discomfort. Symptoms also present at rest. If any physical activity is undertaken, discomfort increases.

AHA/ACC 2009 - Staging System of Heart Failure

Stage	Description	Examples
A	People at high risk for developing heart failure but without structural heart disease or symptoms of heart failure. Encompasses “pre heart failure” where intervention with management can overt Progression to symptoms	CAD (coronary artery disease), diabetes, hypertension, metabolic syndrome, obesity, using cardiotoxins or alcohol, family history of cardiomyopathy, cerebrovascular accident (CVA), personal history of rheumatic fever
B	People with structural heart disease but without signs and symptoms of heart failure NYHA Class I	Left ventricular hypertrophy (LVH) or reduced left ventricular ejection fraction (LVEF), asymptomatic valvular heart disease, previous MI
C	People with structural heart disease with prior or current symptoms of heart failure NYHA Class II and III	Known structural heart disease with dyspnea, fatigue, inability to exercise
D	People who have advanced heart failure and severe symptoms difficult to manage with standard treatment NYHA Class IV	Marked symptoms at rest despite maximal medical therapy, with recurrent hospitalizations

ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

Main Focus

- ***Pharmacological Therapy for HFrEF***
  - ***Beta Blockers***
  - ***ACEi / ARB/ ARNI***
  - ***Hydralazine/ Isosorbide***
  - ***Aldosterone Antagonist***
  - ***SGLT-2 Inhibitor***
  - ***Soluble Guanylate Cyclase Stimulator***

Comorbidities and Treatment

- ***HTN***
- ***Anemia/ Iron Deficiency***
- ***Sleep Disturbances***
- ***Exercise***

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Comorbidities and Treatment

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- ***Anemia/ Iron Deficiency***
- ***Sleep Disturbances***
- ***Exercise***

Exercise As Medicine

- A vigorous 5-mile walk will do more than all the medicine in the world

  - Paul Dudley White

Exercise as Medicine Used with Permission Jayne Ward, DO Healthy Lifestyles 2019

Contributors to Overall Health Status

- Genetics – 20%
- Environment – 20%
- Access to health care – 10%
- Behavior – 50%

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Activity vs. Fitness

- Activity
  - Movement carried out by skeletal muscles that requires energy
- Fitness
  - Ability to carry out tasks without undue fatigue
- Exercise
  - Planned, structured, repetitive and intentional movement intended to improve fitness
- Exercise capacity
  - Cardiorespiratory fitness or VO2 max

Exercise as Medicine Used with Permission Jayne Ward, DO Healthy Lifestyles 2019

Exercise Capacity

- Measured in metabolic equivalents – METS
- 1 MET is the resting metabolic rate
- Highly trained endurance athletes have exercise capacity of 25 METS
- Strong predictor of all cause mortality
  - Association is stronger than that for smoking, HTN, DM and hyperlipidemia

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Exercise Capacity

Leisure Time Activity	MET - Hours
Normal pace walking 2-2.9 mph	3
Brisk pace walking 3-3.9 mph	4
Very brisk pace walking 4 + mph	4.5
Jogging (slower than 10 min/mile)	7
Running (faster than 10 min/mile)	12
Bicycling	7
Tennis/Squash/Racquetball	7
Lap swimming	7
Stair climber	8
Yoga, stretching, toning	4
Lawn mowing	6

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Exercise Capacity

- Increase of 1 MET reduces mortality
  - 17% in women
  - 12% in men
- It takes a person with poor fitness 12 weeks to increase fitness by 1 MET

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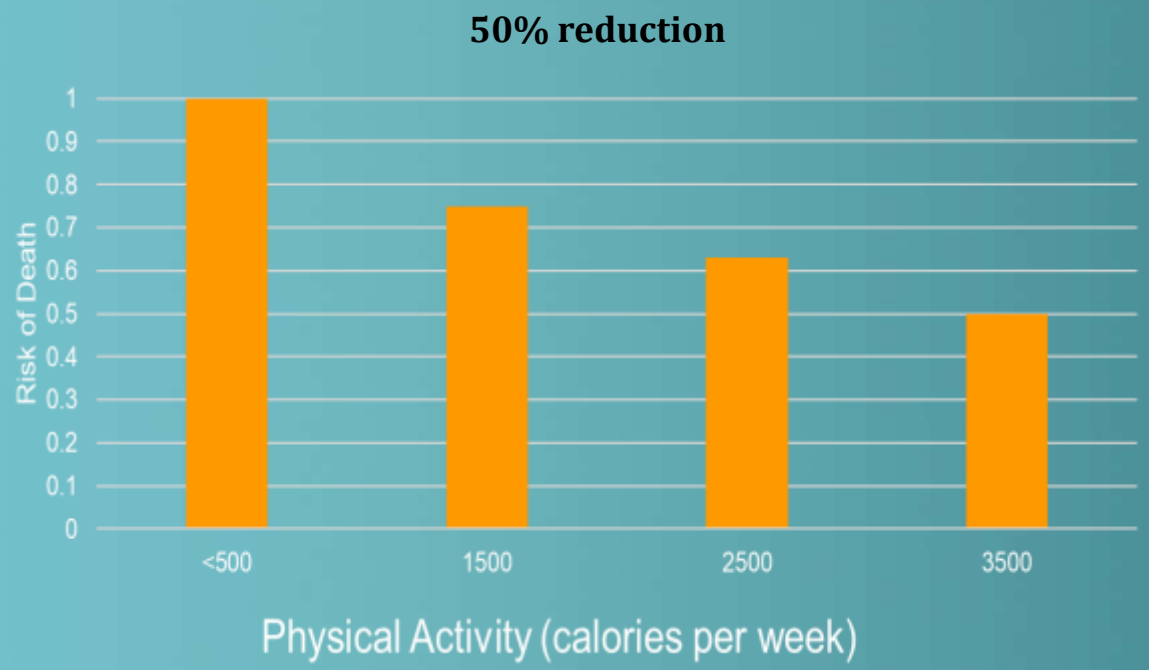
How Healthy is Exercise?
Harvard Alumni study – Cardiac Deaths



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Why We Don't Do It…

- Inadequate education
  - 7 studies – most common barriers
    - Lack of time
    - HCP perception of lack of efficacy
    - Lack of knowledge
    - Patient comorbidities
  - Only 32% of HCP professionals believe their advice will change behavior
  - No medical student curriculum
- Study of IM residents – 90% thought it was the physician's responsibility
  - Only 15% actually provided counselling

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What About Exercise In Our Heart Failure Patients?

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Exercise Therapy in Advanced Heart Failure

Background

- Despite a variety of pharmacological and device therapies for persons with chronic heart failure (HF), prognosis and quality of life (QOL) remain poor.
- The need for new effective strategies to improve outcomes for patients with HF is underscored by persistently high mortality, morbidity, healthcare use, and costs associated with HF, with >1 million US HF hospitalizations. [1]

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https://www.ahajournals.org/doi/10.1161/CIRCHEARTFAILURE.113.001420

Exercise Therapy in Advanced Heart Failure

- **Exercise intolerance** is a primary symptom in patients with chronic HF, both those with preserved ejection fraction (HFpEF) and reduced ejection fraction (HFrEF), and is a strong determinant of prognosis and of reduced QOL.[2]

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Exercise Therapy in Advanced Heart Failure

- **Exercise training** improves exercise intolerance and QOL in patients with chronic stable HFrEF, and has become an accepted adjunct therapy for these patients (Class B level of evidence) based on a fairly extensive evidence base of randomized trials, mostly small.[3]

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Exercise Therapy in Advanced Heart Failure

So what happens in patients with HF?

- To help redirect available blood flow and maintain arterial pressure during exercise in patients with HF, muscles experience enhanced sympathetic vasoconstriction, downregulation of endothelial vasodilatory function, and elevated venous pressures that impair the muscle pumping action to facilitate blood flow

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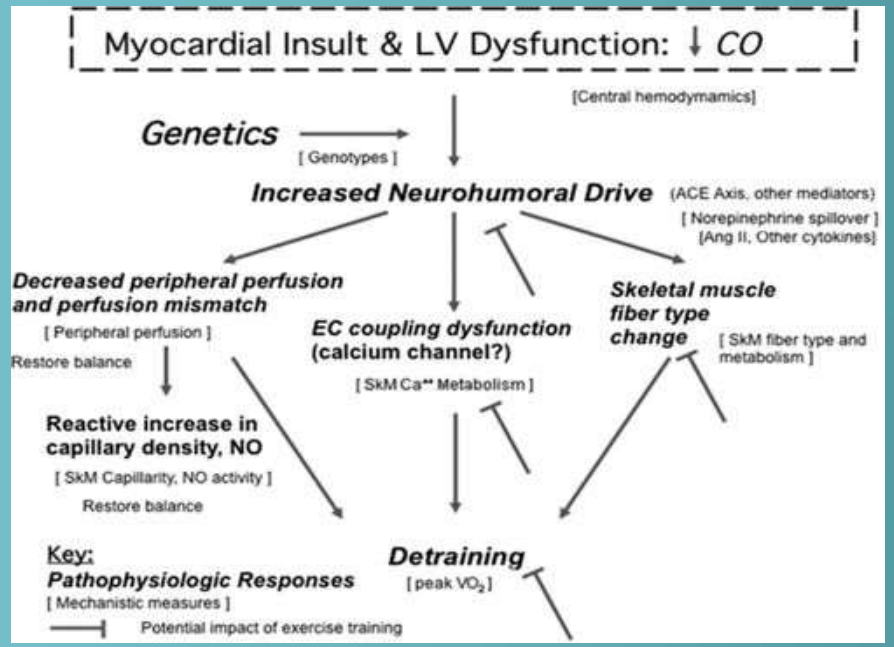
Exercise Therapy in Advanced Heart Failure



- The figure represents a model of how left ventricular systolic dysfunction, induced by a myocardial insult with decreased CO, can lead to impaired exercise tolerance and how exercise training may reverse such changes.

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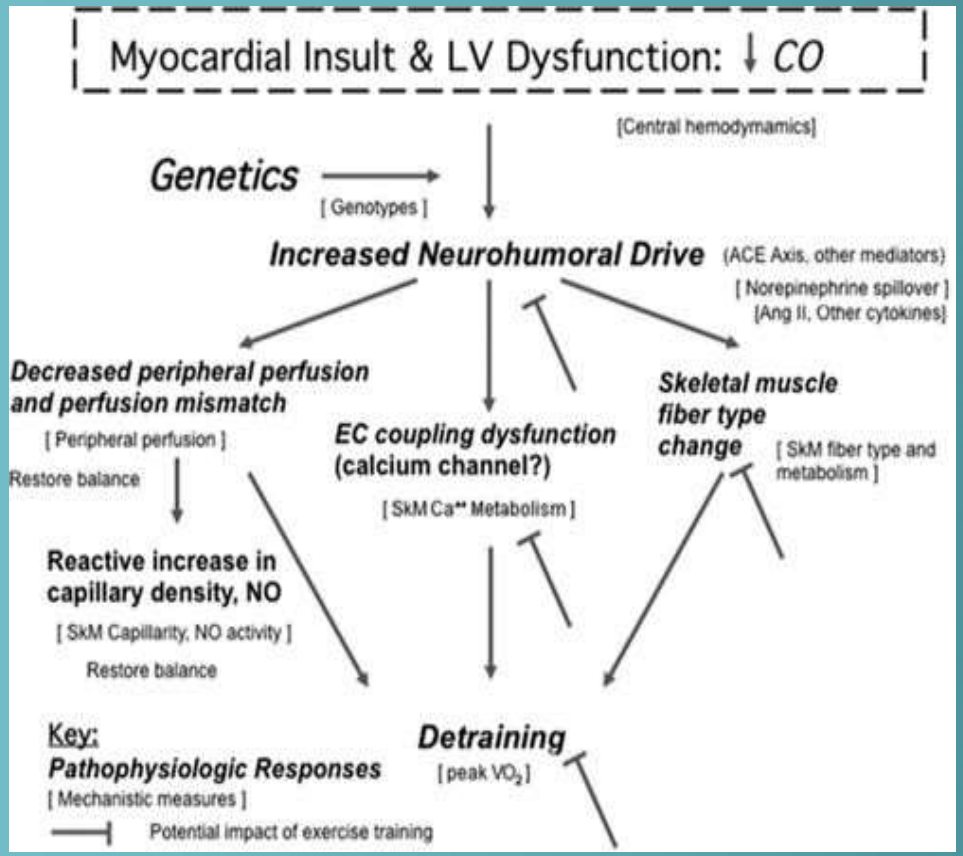

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Jerome L. Fleg. Circulation: Heart Failure. Exercise Training as Therapy for Heart Failure, Volume: 8, Issue: 1, Pages: 209-220, DOI: (10.1161/CIRCHEARTFAILURE.113.001420)

Exercise Therapy in Advanced Heart Failure

What can exercise accomplish in HF patient?

- A therapeutic program that improves skeletal muscle O_2 delivery, while simultaneously improving mitochondrial and contractile efficiency might substantially improve metabolic function and exercise tolerance in patients with HF.

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Exercise Therapy in Advanced Heart Failure

Unfortunately, as we age, so does our exercise capacity. So what effect does aging, frailty, and comorbidities have on our exercise ability?

- Progressive decline in exercise capacity and decreased physiological reserve in cardiovascular function as well as in most other organ systems, altered pharmacological responses, increased adverse effects of medical therapy often lead to prolonged and often incomplete recovery.

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Exercise Therapy in Advanced Heart Failure

Unfortunately, most studies focus on younger patients.

- The prevalence and incidence of HF increase sharply after middle age.[1]
- Approximately 88% of HF deaths and >75% of HF hospitalizations occur in patient's aged ≥65 years.[40]
- Despite these demographics, older persons are significantly under-represented in HF studies, especially those involving exercise training.[41,42]

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Exercise Therapy in Advanced Heart Failure

Unfortunately, most studies focus on younger patients.

- In an analysis of 59 general HF trials conducted from 1985 to 1999 in >45 000 patients, the average age of participants was 61.4 years, whereas it is >77 years in the community.[42] In the HF-ACTION trial, the largest trial of exercise training in HF, the mean age of participants was 59.5 years.[4]

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Exercise Therapy in Advanced Heart Failure

Efficacy and Safety of Exercise Training in Patients With Chronic Heart Failure: HF-ACTION Randomized Controlled Trial

- Christopher M. O'Connor, MD, David J. Whellan, MD, MHS, Kerry L. Lee, PhD, Steven J. Keteyian, PhD, Lawton S. Cooper, MD, MPH, Stephen J. Ellis, PhD, Eric S. Leifer, PhD, William E. Kraus, MD, Dalane W. Kitzman, MD, James A. Blumenthal, PhD, David S. Rendall, PA-C, Nancy Houston Miller, RN, BSN, Jerome L. Fleg, MD, Kevin A. Schulman, MD, Robert S. McKelvie, MD, PhD, Faiez Zannad, MD, PhD, and Ileana L. Piña, MD, for the HF-ACTION Investigators

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure

- Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training **(HF-ACTION)** trial compared an individualized, supervised, and home-based aerobic exercise program plus guideline-based pharmacological and device therapy with guideline-based therapy alone in persons with HFrEF.

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Exercise Therapy in Advanced Heart Failure

Context

- Guidelines recommend that exercise training be considered for medically stable outpatients with heart failure. Previous studies have not had adequate statistical power to measure the effects of exercise training on clinical outcomes.

Objective

- To test the efficacy and safety of exercise training among patients with heart failure.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure

Design, Setting, and Patients

- Multicenter, randomized controlled trial among 2331 medically stable outpatients with heart failure and reduced ejection fraction. Participants in Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) were randomized from April 2003 through February 2007 at 82 centers within the United States, Canada, and France; median follow-up was 30 months.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure

Characteristics	No. (%) of Patients[a]	
	Usual Care (n = 1172)	Exercise Training (n = 1159)
Age, median (IQR), y	59.3 (51.1–68.2)	59.2 (51.2–67.8)
Female sex	314 (26.8)	347 (29.9)
Hispanic or Latino ethnicity	48 (4.1)	40 (3.5)
Race		
Black or African American	372 (31.7)	377 (32.5)
White	728 (62.1)	698 (60.2)
Other	56 (4.8)	65 (5.6)
NYHA class		
II	754 (64.3)	723 (62.4)
III	409 (34.9)	422 (36.4)
IV	9 (0.8)	14 (1.2)
Ischemic etiology of heart failure	599 (51.1)	598 (51.6)
Left ventricular ejection fraction, median (IQR), %	24.9 (20.0–30.2)	24.6 (20.0–30.0)
Diabetes mellitus	370 (31.6)	378 (32.6)
Previous myocardial infarction	499 (42.6)	480 (41.4)
Hypertension	676 (57.7)	712 (61.4)
Atrial fibrillation or atrial flutter	241 (20.6)	247 (21.3)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

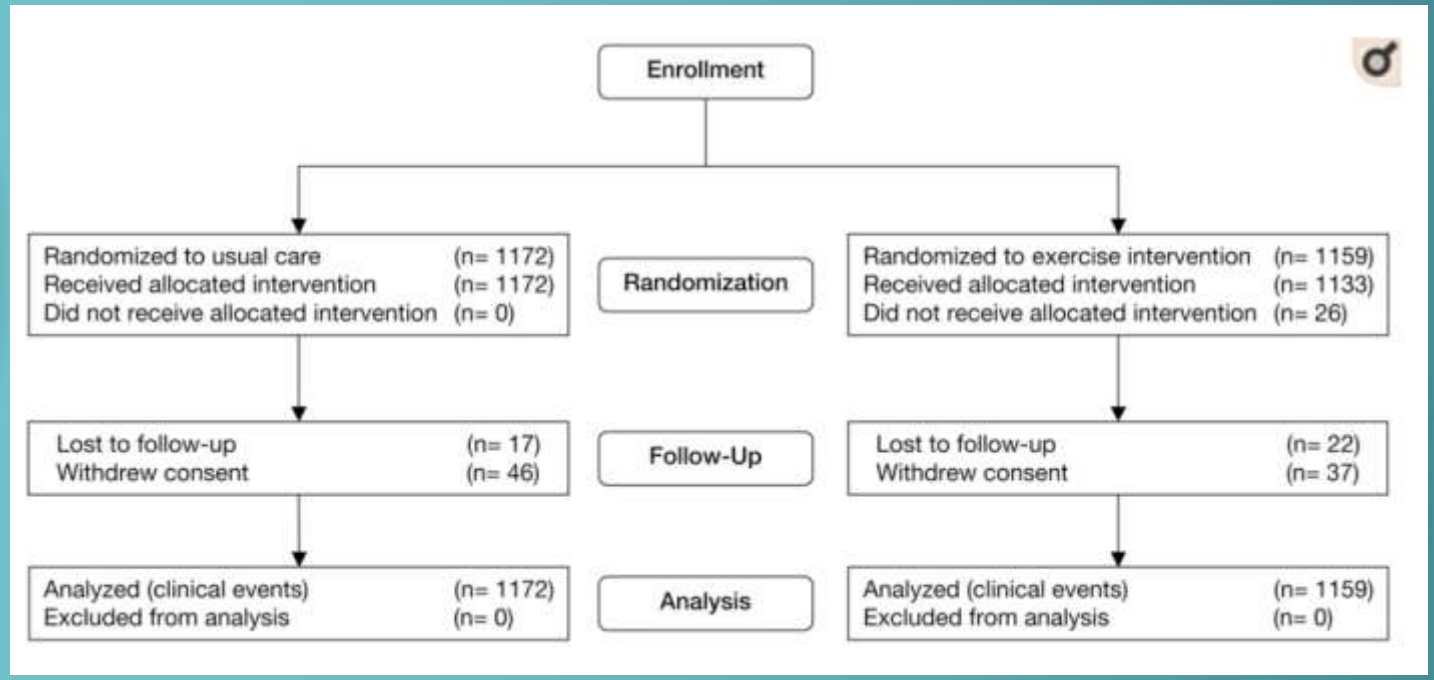
Exercise Therapy in Advanced Heart Failure

Exercise Training Protocol

- 3 sessions per week for a total of 36 sessions in 3 months.
- During the supervised training phase, patients performed walking, treadmill, or stationary cycling as their primary training mode.
- Exercise was initiated at 15 to 30 minutes per session at a heart rate corresponding to 60% of heart rate reserve (maximal heart rate on cardiopulmonary exercise test minus resting heart rate).
- After 6 sessions, the duration of the exercise was increased to 30 to 35 minutes, and intensity was increased to 70% of heart rate reserve.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure



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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure

Subjects With Selected Adverse Events

Adverse Event	Usual Care (N = 1171)[a]	Exercise Training (N = 1159)
Prespecified Cardiovascular Adverse Events		
Worsening heart failure, No. (%)	340 (29.0)	303 (26.1)
Myocardial infarction, No. (%)	45 (3.8)	41 (3.5)
Unstable angina, No. (%)	88 (7.5)	86 (7.4)
Serious adverse arrhythmia, No. (%)[b]	164 (14.0)	167 (14.4)
Stroke, No. (%)	28 (2.4)	33 (2.8)
Transient ischemic attack, No. (%)	23 (2.0)	20 (1.7)
Any of the above events, No. (%)	471 (40.0)	434 (37.4)
General Adverse Events		
Hospitalization for fracture of the hip or pelvis, No. (%)	7 (0.6)	3 (0.3)
Outpatient fracture repair, No. (%)	20 (1.7)	13 (1.1)
ICD firing, No. fired/No. with ICD (%)	151/644 (23.0)	142/641 (22.2)
Hospitalization after exercise, No. (%)[c]	22 (1.9)	37 (3.2)
Death after (or unknown if after) exercise, No. (%)[d]	5 (0.4)	5 (0.4)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure

Clinical Events

Event	Usual Care (N = 1171)[a]	Exercise Training (N = 1159)	Hazard Ratio (95% CI)	*P* Value
All-cause mortality or all-cause hospitalization (primary end point), No. (%)	796 (68)	759 (65)	0.93 (0.84–1.02)	.13
Cardiovascular mortality or cardiovascular hospitalization, No. (%)	677 (58)	632 (55)	0.92 (0.83–1.03)	.14
Cardiovascular mortality or heart failure hospitalization, No. (%)	393 (34)	344 (30)	0.87 (0.75–1.00)	.06
Cardiovascular mortality or heart failure hospitalization or cardiac transplantation or left ventricular assist device, No. (%)	403 (34)	353 (30)	0.87 (0.75–1.00)	.06
All-cause mortality, all-cause hospitalization, emergency department visit, or urgent clinic visit for heart failure exacerbation, No. (%)	906 (77)	885 (76)	0.99 (0.90–1.08)	.79
All-cause mortality, No. (%)	198 (17)	189 (16)	0.96 (0.79–1.17)	.70
Cardiovascular mortality, No. (%)	143 (12)	131 (11)	0.92 (0.74–1.15)	.47

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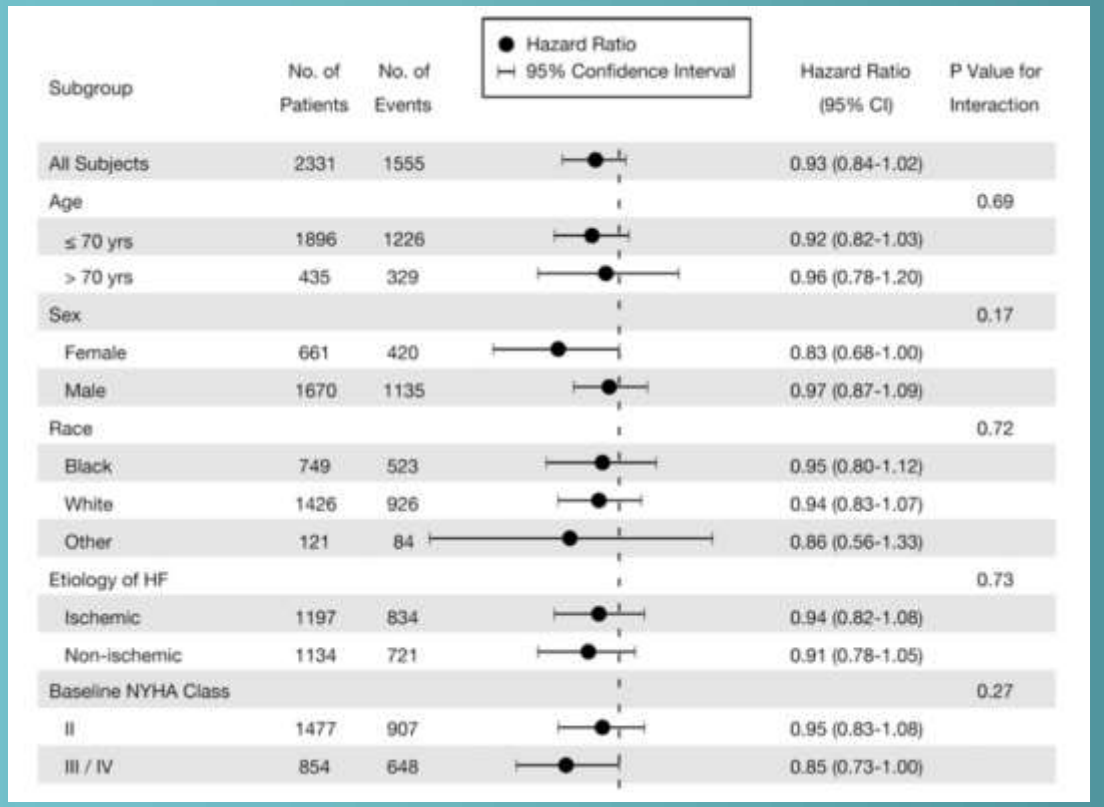
Exercise Therapy in Advanced Heart Failure



Subgroup	No. of Patients	No. of Events	Hazard Ratio (95% CI)	P Value for Interaction
All Subjects	2331	1555	0.93 (0.84-1.02)	
Age				0.69
≤ 70 yrs	1896	1226	0.92 (0.82-1.03)	
> 70 yrs	435	329	0.96 (0.78-1.20)	
Sex				0.17
Female	661	420	0.83 (0.68-1.00)	
Male	1670	1135	0.97 (0.87-1.09)	
Race				0.72
Black	749	523	0.95 (0.80-1.12)	
White	1426	926	0.94 (0.83-1.07)	
Other	121	84	0.86 (0.56-1.33)	
Etiology of HF				0.73
Ischemic	1197	834	0.94 (0.82-1.08)	
Non-ischemic	1134	721	0.91 (0.78-1.05)	
Baseline NYHA Class				0.27
II	1477	907	0.95 (0.83-1.08)	
III / IV	854	648	0.85 (0.73-1.00)	

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure

- Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training **(HF-ACTION)** trial compared an individualized, supervised, and home-based aerobic exercise program plus guideline-based pharmacological and device therapy with guideline-based therapy alone in persons with HFrEF.
- **The exercise arm showed a modest reduction in cardiovascular hospitalizations and mortality and improved QOL.[4,5] .**

https://www.ahajournals.org/doi/10.1161/CIRCHEARTFAILURE.113.001420

Exercise Therapy in Advanced Heart Failure

Unfortunately, this landmark study leaves several unanswered key questions:

- including the role of exercise dose;
- the relative benefit of different types of aerobic exercise, including high-intensity interval training (HIIT), and resistance, training relative to aerobic training;
- combination of exercise training with other therapies;
- optimization of adherence;
- benefit for older patients with HF, those with HFpEF or multiple comorbidities, and those with acute decompensated HF.

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What about exercise therapy in patients with heart failure with preserved left ventricular function (HFpEF)?

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Exercise Therapy in patients with Heart Failure with preserved left ventricular function (HFpEF)

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Abstract

Background

Assessment and Quantitation of Exercise Intolerance in HFpEF

Mechanisms of Exercise Intolerance in Chronic HFpEF and Benefits From Exercise Training

Critical Analysis of

Supervised Exercise Training for Chronic Heart Failure With Preserved Ejection Fraction: A Scientific Statement From the American Heart Association and American College of Cardiology

Vandana Sachdev, Kavita Sharma, Steven J. Keteyian, Charina F. Alcain, Patrice Desvigne-Nickens, Jerome L. Fleg, Viorel G. Florea, Barry A. Franklin, Maya Guglin, Martin Halle, Eric S. Leifer, Gurusher Panjrath, Emily A. Tinsley, Renee P. Wong, Dalane W. Kitzman and ... See all authors

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Other version(s) of this article

Abstract

Heart failure with preserved ejection fraction (HFpEF) is one of the most common forms of heart failure; its prevalence is increasing, and outcomes are worsening. Affected patients often experience severe exertional dyspnea and debilitating fatigue, as well as poor quality of life, frequent hospitalizations, and a high mortality rate. Until recently, most pharmacological intervention trials for HFpEF yielded neutral primary outcomes. In contrast, trials of exercise-based interventions have consistently demonstrated large, significant, clinically meaningful improvements in symptoms, objectively determined exercise capacity, and usually quality of life. This success may be attributed, at least in part, to the pleiotropic effects of exercise, which may favorably affect the full range of abnormalities—peripheral vascular, skeletal muscle, and cardiovascular—that contribute to exercise intolerance in HFpEF. Accordingly, this scientific statement critically examines the currently available literature on the effects of exercise-based therapies for chronic stable HFpEF, potential mechanisms for improvement of exercise capacity and symptoms, and how these data compare

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https://www.ahajournals.org/doi/10.1161/CIR.0000000000001122

Exercise Therapy in patients with Heart Failure with preserved left ventricular function (HFpEF)

A new version of the American College of Cardiology/American Heart Association guidelines for HF management was recently released

HFpEF treatment recommendations have been added for sodium-glucose cotransporter 2 inhibitors (Class of Recommendation 2a), mineralocorticoid receptor antagonists (Class of Recommendation 2b), and angiotensin receptor neprilysin inhibitors (Class of Recommendation 2b).[2]

Current guidelines also include a Class 1 recommendation (Level of Evidence A) for exercise training in patients with HF.[2] Although this recommendation does not distinguish between HFpEF and HFrEF

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New Recommendations for Heart Failure with preserved left ventricular function (HFpEF)

COR	LOE	Recommendations
2a	B - R	In patients with HFpEF, **SGLT2i** can be beneficial in decreasing HF hospitalizations and cardiovascular mortality
2b	B - R	In selected patients with HFpEF, **MRAs** may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum
2b	B - R	In selected patients with HFpEF, **ARNi** may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum

2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure - DOI: 10.1016/j.cardfail.2022.02.010

HFSA

JCF Journal of Cardiac Failure

Heidenreich PA, *et al. J Card Fail* 2022

JHFS

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https://m2.healio.com/~/media/learningsites/learntheheart/assets/4/f/9/0/atrialfibrillation.jpg

Exercise Therapy in patients with Heart Failure with preserved left ventricular function (HFpEF)

Several pathophysiological mechanisms are responsible for the severely reduced aerobic exercise capacity in patients with HFpEF.

These can be broadly categorized as **cardiac, pulmonary, vascular, and skeletal muscle**.

Other factors include **sedentary behavior; atrial fibrillation**, which is accompanied by a worse prognosis[10,42]; and **obesity,** which may be associated with increased plasma volume, cardiac remodeling, and potentially pericardial restraint.[43]

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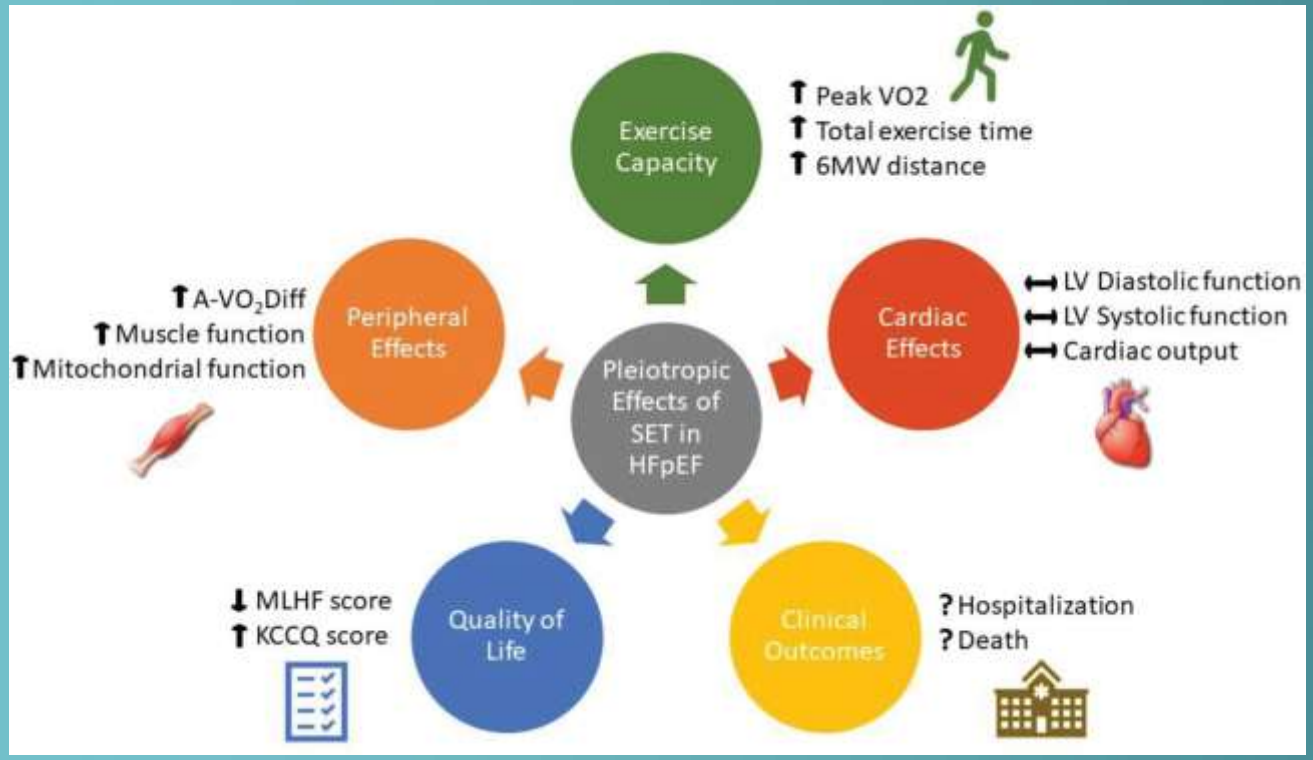
Exercise Therapy in patients with Heart Failure with preserved left ventricular function (HFpEF)



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Exercise Therapy in patients with Heart Failure with preserved left ventricular function (HFpEF)

Table 1. RCTs of Facility-Based SET in HFpEF

Study author, year	Aim of study	Study size: exercise/control (blinded: yes/no)	Centers, n	Patient population	Type of ET	SET program	Primary end points (unless otherwise noted)
Kitzman et al,[87] 2010	To evaluate the effect of ET on peak Vo_2 and QOL	26 ET/27 control (yes)	1	EF ≥50%, NYHA II–III, age 70±6 y, 17% male	Walking	3 times per wk for 4 mo	Improved peak Vo_2, ex test time, 6MWD
Edelmann et al,[88] 2011	To evaluate the effect of ET on functional capacity, cardiac function, and QOL	44 ET/20 control (yes)	3	EF ≥50%, NYHA II–III, age 64±8 y, 45% male	Bike+resistance	3 times per wk, 35 min each, for 6 mo	Improved peak Vo_2, ex test time, 6MWD
Smart et al,[89] 2012	To evaluate the effect of ET on functional capacity, cardiac function, and QOL	14 ET/18 control (echo blinded; not mentioned for exercise testing)	2	EF >45%, NYHA II–III, age 67±5 y, 58% male	Bike	3 times per wk, 30 min each, for 4 mo	Improved peak Vo_2
Kalliatakou et al,[71] 2014	To compare dancing vs ET vs control on functional capacity	18 dancing, 17 ET/16 control (yes)	1	EF ≥40%, NYHA II–III, age 67±7 y, 100% male	Greek dance vs bike/treadmill+resistance vs control	3 times per wk, 30 min each, for 1 mo	Both dancing and ET improved peak Vo_2 vs test time
Fu et al,[79] 2018	To explore how aerobic interval training affects central and peripheral hemodynamics	30 ET/29 control (echo blinded; not mentioned for exercise testing)	1	HFpEF, HFrEF, 2 control groups; EF ≥50%, NYHA II–III, age 61±3 y, 87% male	Bike (3-min intervals)	3 times per wk, 30 min each, for 3 mo	Improved peak Vo_2
Kitzman et al,[81] 2016	To determine whether caloric restriction or SET improves exercise capacity and QOL	46 ET/46 control (yes)	1	EF ≥50%, NYHA II–III, age 67±6 y, 20% male, BMI ≥30 kg/m²	2×2 factorial: diet, walking, both, control	3 times per wk, 60 min each, for 3 mo	Improved peak Vo_2, ex test time, 6MWD
Mueller et al,[74] 2021	To compare HIIT, MCT, and guideline-based physical activity on peak Vo_2 change	58 HIIT/58 MCT/60 control (no)	5	EF >50%, HF-high filling pressures and BNP, mean age 70 y, 33% male, mean BMI 30 kg/m²	HIIT cycle (4-min intervals) vs MCT vs control	3 times per wk all, 3 mo SET, follow-up to 12 mo	Improved peak Vo_2 at 3 mo in HIIT and MCT groups

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Exercise Therapy in patients with Heart Failure with preserved left ventricular function (HFpEF)

Types of Exercise Used in Clinical Trials

Exercise studies in patients with chronic, stable HFpEF used various approaches for training, including walking, stationary cycle ergometry, high-intensity interval training (HIIT), strength training, and dancing.[67–73,75–77]

Eleven studies[47,67–72,74–77] used facility-based SET and 4 studies[86–89] used home-based exercise training HIIT studies used 2- to 4-minute exercise bouts with the treadmill or cycle ergometer.[74,76,77]

Although the training frequency was generally 3 sessions per week, the duration ranged from 1 to 8 months, and the intensity of training, when specified, varied considerably (40%–90% of exercise capacity), as did the individual session length (25–60 min).

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Exercise Therapy in patients with Heart Failure with preserved left ventricular function (HFpEF)

Table 2. Critical Gaps in Exercise-Based Therapy in HFpEF

Recommended focus areas for future trials
Setting: supervised, community based, home based, or hybrid
Modalities: HIIT, continuous aerobic training, strength training, or combination
Combination with other lifestyle interventions or medications: dietary weight loss, comprehensive CR, or ET alone
Strategies for long-term adherence: most trials are short-term and long-term maintenance is modest
Strategies to increase accessibility: particularly for underresourced populations
Minimize costs: can specific settings/modalities improve access and minimize costs
Role in management of recently hospitalized, older adults: frailty, impaired balance, and cognition may require innovative interventions
Effect on clinical events (hospitalization, death): larger studies and long-term follow-up are necessary
Preventing the development of HFpEF: supervised or home-based training in patients with multiple risk factors

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What Are The Current Recommendations?

Exercise Therapy in Advanced Heart Failure

Exercise prescription

- It is mandatory that (sub) maximal exercise capacity is measured with a symptom-limited cardiopulmonary exercise test (CPET). A CPET will give information on the degree of cardiac impairment and will objectively measure VO2peak and other prognostic factors (VE/VCO2slope, oscillatory ventilation). Based on the results of CPET, one can:
    - Determine training intensity and perform training adjustments
    - Determine risk and prognosis
    - Re-test after exercise training program to objectify improvement in exercise capacity

https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Exercise-training-as-therapy-for-chronic-heart-failure#:~:text=Conclusions,and%20reduced%20morbidity%20and%20mortality.

Exercise Therapy in Advanced Heart Failure

- A universal agreement on the best training modality in heart failure does not exist.
- Rather, an individualized approach is recommended, based on clinical evaluation and personal preferences.
- Training protocols vary in a number of ways: intensity (aerobic and anaerobic), type (endurance, resistance) and method (continuous and interval).
- Continuous endurance training is the best described form of exercise training and, because of its well-demonstrated efficacy and safety, is highly recommended in the guidelines. It is characterized by a moderate-to-high exercise intensity at steady-state condition of aerobic energetic yield, allowing the patient to perform prolonged training sessions (45-60 min duration). The exercise is usually performed on a bicycle or treadmill.

https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Exercise-training-as-therapy-for-chronic-heart-failure#:~:text=Conclusions,and%20reduced%20morbidity%20and%20mortality.

Exercise Therapy in Advanced Heart Failure

- Resistance/strength training has been proposed to prevent the wasting syndrome and to incorporate upper body exercise, which is important to complete daily life tasks. It is important to prescribe dynamic resistive exercise training of small muscle groups and to avoid Valsalva maneuvers.

https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Exercise-training-as-therapy-for-chronic-heart-failure#:~:text=Conclusions,and%20reduced%20morbidity%20and%20mortality.

Exercise Therapy in Advanced Heart Failure

Setting

- It is recommended to initiate exercise training in a structured, supervised, center-based program. This can be either in-hospital or in a specialized private facility, as long as close supervision and direct monitoring of heart rate and blood pressure are available, especially when HF symptoms are severe. Most center-based programs offer an eight to 12-week training program.
- Thereafter, a gradual transition to a home-based program - with or without telemonitoring tools - is encouraged, stimulating the patient to remain active for a longer time period and to adhere to the exercise training.

https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Exercise-training-as-therapy-for-chronic-heart-failure#:~:text=Conclusions,and%20reduced%20morbidity%20and%20mortality.

Exercise Therapy in Advanced Heart Failure

Special Heart Failure Populations

- ICD and CRT-D patients should start exercise training under medical supervision and monitoring of heart rate. Exercise level and ICD programming should be adapted to keep the maximal heart rate 20 beats below the ICD intervention zone.
- The following patient information should be readily available to reduce the risk of incidents: 1) underlying heart disease and indication of ICD implantation; 2) triggers for arrhythmia (e.g., ischemia) and the arrhythmic substrate; 3) the ICD intervention heart rate; 4) the tachy-therapy that will be delivered.

https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Exercise-training-as-therapy-for-chronic-heart-failure#:~:text=Conclusions,and%20reduced%20morbidity%20and%20mortality.

Exercise Therapy in Advanced Heart Failure

Conclusion

- Regular exercise training in patients with HFrEF and HFpEF was safe.
- Exercise training produced a nonsignificant reduction in the primary end point (all-cause mortality or all-cause hospitalization) and key secondary clinical end points.
- The treatment effect was statistically significant for the primary end point and for the secondary end point of cardiovascular mortality or heart failure hospitalization.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure

Conclusion

- These findings are consistent with the 33 previous trials and the meta-analyses showing improved outcomes.
- Based on the safety of exercise training and the modest reduction in clinical events in addition to the modest increases in health-related quality of life (reported in the accompanying manuscript by Flynn et al[28]), the HF-ACTION results support a prescribed exercise training program for patients with reduced left ventricular function and heart failure symptoms in addition to evidence-based therapy.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2916661/

Exercise Therapy in Advanced Heart Failure

In addition

- The 2016 European Society of Cardiology heart failure guidelines [8] firmly recommend that:
  - Regular aerobic exercise is encouraged in patients with HF to improve functional capacity and symptoms (Class I indication, level of evidence A); and
  - Regular aerobic exercise is encouraged in patients with HF to reduce the risk of HF hospitalization (Class I indication, level of evidence A).

https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Exercise-training-as-therapy-for-chronic-heart-failure#:~:text=Conclusions,and%20reduced%20morbidity%20and%20mortality.

Thank You For Your Attention!

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