ACC Latin America Conference 2016

MEXICO CITY
OCTOBER 7 - 8, 2016

For more information, visit
ACC.org/LatinAmerica2016

ÚNICA EXPERIENCIA EDUCACIONAL EN TU ÁREA
The Role of Exercise in Management of Patients with Heart Failure

Pamela B. Morris, MD, FACC, FAHA, FASPC, FNLA
Chair, ACC Prevention of Cardiovascular Disease Leadership Council and Section Director, Seinsheimer Cardiovascular Health Program Co-Director, Women’s Heart Care Medical University of South Carolina
Disclosures

• Advisory boards
  – Amgen
  – AstraZeneca
  – Sanofi Regeneron
Heart failure and exercise tolerance

- Variety of non-specific symptoms
- Most frequent: exertional breathlessness
- Fatigue, lethargy, edema
Heart failure and exercise tolerance

• Marked reductions in exercise capacity
• Detrimental effects on activities of daily living
• Health-related quality of life
• Hospital admission rate
• Mortality
What is the evidence for benefit of exercise in HF?
Cardiac rehabilitation in HF

• Definition
  – “The coordinated sum of activities required to influence favorably the underlying cause of CVD, as well as to provide the best possible physical, mental, and social conditions, so that the patients may, by their own efforts, preserve or resume optimal functioning in their community and through improved health behavior, slow or reverse progression of disease.”
  – A central component of CR is exercise training.
Role of Exercise: What is the evidence?

- HFrEF, HFpEF
- Older adults
- Cardiac resynchronization therapy
- Left ventricular assist device
HF-ACTION Trial

- Assessed safety and efficacy of ET for medically stable patients with HFrEF (LVEF \(\leq 35\%\), NYHA class II to IV)
- Large and diverse population (\(n=2331\))
- RCT design
- Optimal medical management including ACEI and BB
- 40% had ICDs and 18% had biventricular pacing
HF-ACTION Trial

• Exercise group
  – Began with 36 supervised training sessions for 30 minutes of exercise 3 days/week
  – Individualized exercise prescription based on CPX
  – At halfway point, received home treadmill or stationary bicycle and heart-rate monitor
  – Instructed to exercise 5 times per week at moderate intensity for 40 minutes

• Usual-care group
  – Given instructions regarding benefits of exercise at moderate intensity for 30 minutes daily
HF-ACTION Trial

• Primary composite endpoint
  – All-cause mortality or all-cause hospital stay

• After median f/u 30 months
  – Non-significant reduction primary combined endpoint
    • HR 0.93, 95% CI: 0.84 to 1.02; p=0.13
  – After adjustment for baseline characteristics predictive of clinical outcomes
    • Duration CPX, LVEF, hx afib, depression
    • HR 0.89, 95% CI: 0.81 to 0.99; p=0.03
  – Secondary endpoint CV mortality or HF hospitalization
    • HR 0.85, 95% CI: 0.74 to 0.99; p=0.03
Efficacy and Safety of Exercise Training in Patients With Chronic Heart Failure: HF-ACTION Randomized Controlled Trial

All-Cause Mortality or All-Cause Hospitalization

HR, 0.93 (95% CI, 0.84-1.02); P = .13
Adjusted HR, 0.89 (95% CI, 0.81-0.99); P = .03a

All-Cause Mortality

HR, 0.96 (95% CI, 0.79-1.17); P = .70

CI indicates confidence interval; HR, hazard ratio.
*Adjusted for key prognostic factors.
Efficacy and Safety of Exercise Training in Patients With Chronic Heart Failure: HF-ACTION Randomized Controlled Trial

CI indicates confidence interval; HR, hazard ratio.

*Adjusted for key prognostic factors.
HF-ACTION Trial

• Subsequent analysis demonstrated that patients who achieved increased exercise volume during the trial had relatively better outcomes
  – Concept of “dose-response” relationship
  – Exercise volume was significant ($p=0.001$) predictor of reduced mortality (all-cause and cardiac) or hospitalization (all-cause or HF)
HF-ACTION Trial

• Criticisms of HF-ACTION
  – Significant benefits after adjustment for predictive factors of the same outcomes
  – Need to extend number of sites to achieve enrollment goals
    • “ET is inherently problematic”
  – Adherence to prescribed exercise volume was limited
    • Only 30% exercised at or above target
  – Still leaves residual concerns and questions due to limited enrollment and suboptimal adherence
HF-ACTION Trial

• Criticisms of HF-ACTION
  – Participants could not be enrolled until 6 weeks after hospitalization
    • Safety of earlier enrollment to reduce readmission is unknown
  – CPX and 6-minute walk as metrics to assess ET efficacy, safety, and stability
    • Many see this as barrier to implementation
    • Options to use exercise assessments more selectively to make ET more accessible and uncomplicated in relatively stable subsets of HF patients
  – Few adults >75 years of age, limited exercise modalities, HFpEF, LVADs
Heart failure and exercise-based rehabilitation: Cochrane Review 2014

• 33 RCTs with 4740 participants
  • Included both HF_{r}EF and HF_{p}EF, primarily NYHA classes II and III
  • Exercise-based rehabilitation versus no-exercise control
  • At least 1-year follow-up

• Small body of evidence for HF_{p}EF
  • 3 trials

Heart failure and exercise-based rehabilitation: Cochrane Review 2014

• No difference in pooled mortality between exercise-based rehabilitation vs. no exercise control in trials with up to 1 year f/u
  • RR 0.93, 95% CI 0.69 to 1.27
  • However, there was trend toward reduction in mortality in trials with >1 year f/u (RR 0.88, 95% CI 0.75 to 1.02)
• ET reduced rate of overall and HF specific hospitalizations
  • RR 0.61, 95% CI 0.46 to 0.80
• Significant improvement in in QOL measures
• Independent of age, gender, LF dysfunction, type of CR, dose of exercise, length of f/u

Heart failure and exercise-based rehabilitation: Cochrane Review 2014

• Conclusions
  • ET does not increase or decrease risk of all-cause mortality in short-term (1-year)
  • ET reduces the risk of hospital admissions
  • ET confers important improvements in health-related quality of life
  • May reduce mortality in the longer term
  • Benefits consistent across participant characteristics
  • Further RCT evidence needed for HFpEF

Exercise in HFpEF

• HFpEF now approximately 54% of patients presenting with HF

• Dual effects of intrinsic age-related susceptibility to HFpEF and the expanding older adult population, as well as high prevalence of associated comorbidities (HTN, DM, afib, obesity)

• Severe exercise intolerance is the principal clinical feature in HFpEF (measured as decreased peak VO$_2$)
Exercise in HFpEF

• 2016 systematic review of RCTs comparing ET in patients with HFpEF

• 7 published studies
  – 279 patients, 157 allocated to ET/122 allocated to control
  – NYHA class I-III
  – LVEF >45%
  – Different exercise training modalities/protocols
Exercise in HFpEF

- Improvement in peak VO$_2$
- Some showed improvement in QOL scores
- Variable effects on echocardiographic variables
- No consistent effect on BNP or surrogate endpoints (EC function, arterial stiffness)
- No studies designed to analyze CV outcomes
- No serious adverse events
- Findings contrast with robust information available on ET for HFrEF patients (30 trials with >4000 patients)
Exercise in HFpEF

- Data limited by few trials, few patients
- Heterogeneous interventions
- Heterogeneous criteria for defining HFpEF
- Heterogeneous populations
- Varying endpoints
Exercise in older adults with HF

- National Institute on Aging REHAB-HF (Trial of Rehabilitation Therapy in Older Acute Heart Failure Patients)
  - Older adults with acute decompensated HFpEF and HFrEF (age ≥60 years, n=360)
  - Randomized in a 1:1 fashion to 12-week novel, progressive, multi-domain rehabilitation and exercise training intervention or attention control
  - Endurance, mobility, strength, and balance training
  - 3 times per week in an outpatient setting
  - Control arm will receive all services ordered by their primary physician and will be contacted bi-weekly by study staff.
  - Measures of physical function and quality of life at baseline, 1 month, and 3 months. Clinical events monitored for 6 months following the index hospitalization.

http://clinicaltrials.gov/ct2/show/NCT02196038
Exercise in older adults with HF

• National Institute on Aging REHAB-HF (Trial of Rehabilitation Therapy in Older Acute Heart Failure Patients)
  – Primary outcome is improved physical function
  – Secondary outcome is re-hospitalization
  – Other assessments include frailty, multi-morbidity, polypharmacy, and other age-related complexities of care
Exercise in patients with LVADs: REHAB-VAD RCT

- Enrolled subjects
  - n=26; 7 women; mean age 55 years; mean LVEF 21%
- Assessments:
  - Symptom limited CPX,
  - Kansas City Cardiomyopathy Questionnaire (KCCQ)
  - 6-min walk test
  - Single-leg isokinetic strength test
- 2:1 randomization to CR versus usual care
- CR group: 18 visits of aerobic exercise at 60% to 80% of heart rate reserve.
Cardiac Rehabilitation Improves Functional Capacity and Patient-Reported Health Status in Patients With Continuous-Flow Left Ventricular Assist Devices: The Rehab-VAD Randomized Controlled Trial

Peak VO2 for Subjects in Both the CR and Usual Care Groups

Lines represent change over time for each patient. Darker lines indicate average change over time for both groups.
Cardiac Rehabilitation Improves Functional Capacity and Patient-Reported Health Status in Patients With Continuous-Flow Left Ventricular Assist Devices: The Rehab-VAD Randomized Controlled Trial

Kansas City Cardiomyopathy Questionnaire Summary Score for CR and Usual Care Group Subjects
For CR group, changes at follow-up were significant (*p = 0.001) and significantly different from changes in the usual care group (†p = 0.005).

Single Leg Isokinetic Strength Measures for CR and Usual Care Group Subjects
The change at follow-up was significant in the CR group (*p = 0.003) and significantly different from changes in the usual care group (†p = 0.016).
Exercise in patients with LVADs: REHAB-VAD RCT

• Improvements in CR group
  • Peak oxygen uptake
  • Treadmill time
  • Kansas City Cardiomyopathy Questionnaire score
  • 6 minute walk distance
  • Leg strength

• Need future trials of outcomes
Exercise in patients with LVADs

- Improved survival, functional capacity, health status
- Many patients still experience exercise intolerance and HF-related symptoms.
- Careful, structured, medically supervised exercise-based training is advocated.
- Address challenges that influence quality of life and independence
- As durability of LVADs improve and duration of support is extended, optimization of functional capacity and health status is critical.
Exercise in HF patients with CRT

- >50% patients with HF have implanted pacemaker or ICD
- Few longitudinal data on exercise and outcomes in patients with implanted cardiac rhythm devices
- Even less known about ET in patients with RV vs. BiV pacing
- Analysis of HF-ACTION trial in patients with pacemakers, ICDs, and BiV pacemakers (n=1118, 48%)
  - 435 with BiV pacemakers or BiV ICDs

J Cardiac Fail. 2015;21:60-67
Exercise in HF patients with CRT

- Patients with devices were older, more frequently white, and had lower peak VO$_2$.
- Peak VO$_2$ improved similarly with ET in groups with and without pacing devices.
- Primary composite endpoint—death or hospitalization—reduced only in patients randomized to ET without a device.
  - HR 0.79, 95% CI 0.67 to 0.93; p=0.004

ET may improve exercise capacity in patients with implanted cardiac devices, but beneficial effects on hospitalization or death may be attenuated.
Exercise in HF patients with CRT

- 52 patients with CRT-D
- NYHA class III
- N=26 underwent ET in hospital and continued home program with telemonitoring 5 times per week
- N=26 had hospital rehab but no home training program
- CRT-EX group achieved better peak VO$_2$, peak and treadmill test duration at 3-4 months
- Benefits not sustained at 12- and 18-month f/u
Exercise in HF patients with CRT

• Safe option for additional treatment
• Improved physical fitness
• Improved QOL measures
• Benefits not sustained
• No impact on mortality or hospitalization rates
Guidelines for Management of HF

• ACCF/AHA 2013
• ESC 2012
• NICE 2010
• All consistently recommend CR as an effective and safe intervention in HF.
Guidelines for Management of HF

• ACCF/AHA 2013
  – Class I
  • Exercise training (or regular physical activity) is recommended as safe and effective for patients with HF who are able to participate to improve functional status. (Level of evidence: A)
Guidelines for Management of HF

• ACCF/AHA 2013
  – Class IIa
  • Cardiac rehabilitation can be useful in clinically stable patients with HF to improve functional status, exercise duration, health-related quality of life, and mortality. (Level of evidence: B)
Guidelines for Management of HF

• ACCF/AHA 2013
  – Exercise training is safe and has numerous benefits.
  – CR reduces mortality, improves functional capacity, exercise duration, and HRQOL.
  – CR reduces hospitalizations.
  – Improves EC function, blunts catecholamine spillover, and increases peripheral oxygen extraction.
Guidelines for Management of HF

• 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
  • Exercise testing in patients with HF should be considered to optimize prescription of exercise training (preferably cardiopulmonary exercise testing). (IIa C)
  • Combined endurance/resistance training appears safe for patients with HFpEF and HFmrEF and improves exercise capacity (as reflected by an increase in peak oxygen consumption), physical functioning score and diastolic function.
  • Psychosocial intervention and pharmacological treatment are helpful, as well as exercise training, in patients with HFrEF and depression.
Guidelines for Management of HF

- 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
2011 ESC Position Statement: Exercise training in heart failure

• Promotion of common daily activities (brisk walking, climbing stairs, housework, gardening, recreational pursuits)

• Structured physical activity/exercise training
  – Appropriate patient selection (stable NYHA class I-III, early mobilization after acute exacerbation)
  – Training protocol identification
  – Exercise intensity
  – Monitoring of progression
Exercise training in heart failure: from theory to practice. A consensus document of the HFA and the EACPR

Table 1 Summary of contraindications to exercise testing and training (A), exercise training (B), and increased risk for exercise training (C)

(A) Contraindications to exercise testing and training
1. Early phase after acute coronary syndrome (up to 2 days)

(B) Contraindications to exercise training
1. NYHA functional class IV
2. Complex ventricular arrhythmia at rest or appearing with exertion
3. Blood pressure >160/90 mmHg
4. Pre-existing co-morbidities limiting exercise tolerance

(C) Increased risk for exercise training
1. >1.8 kg increase in body mass over the previous 1–3 days
2. Concurrent, continuous, or intermittent diuretic or decongestive therapy
3. Decrease in systolic blood pressure with exercise
4. NYHA functional class IV
5. Complex ventricular arrhythmia at rest or appearing with exertion
6. Supine resting heart rate >100 b.p.m.
2011 ESC Position Statement:  
Exercise training in heart failure

• Specific populations  
  – Implantable cardioverter defibrillators  
  – Cardiac resynchronization therapy

• Limited literature  
  – Real-world experience shows ET can be performed safely
2011 ESC Position Statement: Exercise training in heart failure

- Recommend symptom-limited CPX
  - Chronotropic response to exercise
  - Exercise-induced arrhythmias
  - Effectiveness of pharmacological heart rate control
  - Risk of reaching HR in the ICD intervention zone

- Begin ET under medical supervision with monitoring
2011 ESC Position Statement: Exercise training in heart failure

• Staff caring for patients with ICD should be aware of:
  – Underlying heart disease/etiology
  – Reason for ICD implantation
  – Triggers of arrhythmia (ischemia, specific HRs, etc.)
  – Arrhythmia substrate
  – ICD intervention HR zone
  – Sequence of therapy (monitoring zone, anti-tachycardia pacing, and shock)
2010 NICE Guideline: Chronic heart failure management

• Rehabilitation
  – Offer a supervised group exercise-based rehabilitation programme designed for patients with heart failure.
  – Ensure the patient is stable and does not have a condition or device that would preclude an exercise-based rehabilitation programme.
  – Include a psychological and educational component in the programme.
  – The programme may be incorporated within an existing cardiac rehabilitation programme.
2010 NICE Guideline: Chronic heart failure management

• Rehabilitation
  – The conditions and devices that may preclude an exercise-based rehabilitation programme include:
    • Uncontrolled ventricular response to atrial fibrillation
    • Uncontrolled hypertension
    • High-energy pacing devices set to be activated at rates likely to be achieved during exercise

nice.org.uk/guidance/cg108
Heart Failure and CR: Challenges and Opportunities

- Strong rational for HFrEF
- Persistent underutilization of CR for patients with CHD would suggest the same is likely to be true for HF
- Shifts in US healthcare system seem likely to increase emphasis on CR
- February 2014 CMS decision to include HFrEF as eligible diagnosis for CR payment was import step, but only part of solution
- Additional insights needed regarding HFpEF, older adults, adherence, efficacy, financial feasibility, efficacy
Heart Failure and CR: Challenges and Opportunities

Benefits
- Increases Exercise Capacity
- Improves Risk Factors
- Improves Quality of Life
- Decreases Hospital Admissions
- Promising for Patients with LVADs

Challenges
- Suboptimal Adherence
- Multiple and Complex Comorbidities
- Elderly, Frailty, Disability, Cognitive Deficits
- Exacerbations, Symptoms of Fatigue, Dyspnea
- Logistic Barriers at CR Program Level

Opportunities
- Limited Data on Various Exercise Modalities
- HFpEF Population Less Studied
- More Focus on Prevention in Health Care Industry
- Evaluate enhanced CR Delivery Models
- Research Gaps: Physiology to Public Health Implications

ACC Latin America Conference 2016

MEXICO CITY
OCTOBER 7 - 8, 2016

For more information, visit
ACC.org/LatinAmerica2016

ÚNICA EXPERIENCIA EDUCACIONAL EN TU ÁREA