Cardiac Rehabilitation:
Current and Future Directions

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Disclosures

- There are no conflict of interests related to the products described in this talk
Overview of Talk

- The current state of cardiac rehabilitation
  - Outcome data supporting the use of cardiac rehabilitation
  - Cellular mechanisms associated with exercise
  - Intensive versus traditional cardiac rehabilitation
  - Barriers to utilization of cardiac rehabilitation

- Future directions in cardiac rehabilitation
  - Extending cardiac rehabilitation to the home through digital and wearable technologies to reduce readmission rates
  - Expanding scope of cardiac rehabilitation to HFPEF, POTS, PVD, and microvascular disease

- Our program at UCSD
Cardiac Rehabilitation and Risk Reduction

Time to “Rebrand and Reinvigorate”

Pratik B. Sandesara, MD,* Cameron T. Lambert, MD,* Neil F. Gordon, MD, PhD, MPH,† Gerald F. Fletcher, MD,‡ Barry A. Franklin, PhD,§ Nanette K. Wenger, MD,* Laurence Sperling, MD*

ABSTRACT

Atherosclerotic cardiovascular disease (ASCVD) continues to increase annually in the United States along with its associated enormous costs. A multidisciplinary cardiac rehabilitation (CR) and risk reduction program is an essential component of ASCVD prevention and management. Despite the strong evidence for CR in the secondary prevention of ASCVD, it remains vastly underutilized due to significant barriers. The current model of CR delivery is unsustainable and needs significant improvement to provide cost-effective, patient-centered, comprehensive secondary ASCVD prevention. (J Am Coll Cardiol 2015;65:389-95) © 2015 by the American College of Cardiology Foundation.
Currently Covered Indications for Cardiac Rehabilitation (CR)

- Recent myocardial infarction (within 1 year)
- Post Percutaneous coronary intervention (PCI)
- Coronary artery bypass grafting (CABG)
- Chronic stable angina
- Cardiac transplantation
- Heart valve repair or replacement
- Stable, chronic heart failure (EF<35%)
Outcomes Associated with Cardiac Rehabilitation

- Meta-analysis of 34 randomized controlled trials showed that exercise-based CR programs are associated with:
  - A lower risk of reinfarction (OR 0.53; 95% CI: 0.38 to 0.76)
  - Decreased cardiac mortality (OR 0.64; 95% CI: 0.46 to 0.88)
  - Decreased all-cause mortality (OR 0.74; 95% CI: 0.58 to 0.95)

- CR reduces 90 day hospital readmission rate after acute MI or PCI

- Class IA recommendation by AHA/ACC Guidelines

## Pleiotropic Effects of Cardiac Rehabilitation

### TABLE 1  Potential Cardioprotective Effects of Increased Lifestyle Activity, Structured Exercise, and/or Improved Cardiorespiratory Fitness

<table>
<thead>
<tr>
<th>Category</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-inflammatory</td>
<td>Reduced plasma level of C-reactive protein, which is a biomarker of inflammation (10)</td>
</tr>
<tr>
<td>Antithrombotic</td>
<td>Decreased platelet aggregation (11)</td>
</tr>
<tr>
<td></td>
<td>Enhanced fibrinolysis activity (12)</td>
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<tr>
<td>Antiarrhythmic</td>
<td>Improved cardiac autonomic function (13,14)</td>
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<tr>
<td></td>
<td>Increased vagal tone and decreased sympathetic activity (14)</td>
</tr>
<tr>
<td>Antiatherogenic</td>
<td>Improvement in established ASCVD risk factors</td>
</tr>
<tr>
<td></td>
<td>Improved endothelial function due to increased blood flow and shear stress on arterial walls (15,16)</td>
</tr>
<tr>
<td></td>
<td>Enhanced synthesis and release of nitric oxide, which is responsible for the inhibition of processes involved in atherogenesis (15)</td>
</tr>
<tr>
<td>Improved ASCVD risk factors</td>
<td>Decrease in total cholesterol, LDL-C, and triglycerides (17)</td>
</tr>
<tr>
<td></td>
<td>Increase in HDL-C levels (17)</td>
</tr>
<tr>
<td></td>
<td>Reduced blood pressure (18)</td>
</tr>
<tr>
<td></td>
<td>Increased insulin sensitivity (19)</td>
</tr>
<tr>
<td></td>
<td>Weight reduction (19)</td>
</tr>
<tr>
<td>Anti-ischemic</td>
<td>Improved myocardial perfusion (20)</td>
</tr>
<tr>
<td></td>
<td>Raised ischemic threshold (11)</td>
</tr>
<tr>
<td></td>
<td>Ischemic preconditioning of the myocardium (21)</td>
</tr>
</tbody>
</table>

(J Am Coll Cardiol 2015;65:389–95)
Cellular Mechanisms Associated with Exercise

- Improved mitochondrial function
- Increased nitric oxide production

**Figure 2.** Electron micrographs of cytochrome c oxidase in a patient with severe heart failure (left panel) and in a normal subject (right panel). Enzyme activity within the mitochondria (black) is reduced in heart failure.

Taub  Clin Transl Sci. 2012
Cachexia of Heart Failure

HF patients have:

- Lower capillary density vs. normal subjects (due to low levels of nitric oxide)
- Shifts in muscle fiber types from the oxidative type I to the more glycolytic type II
- Decreases in mitochondrial oxidative enzymes (citrate synthase)
- The muscle wasting typically observed in HF patients, commonly referred to as cachexia, is associated with elevated levels of inflammatory biomarkers

Taub et al, Clin Sci 2013
Exercise Training in CHF: Mortality and Morbidity Effects

- HF-ACTION
- RCT: usual care vs structured exercise training
  - 50 sites in US and Canada with 2331 patients enrolled
- 5 year follow-up
- Outcomes: death, hospitalization

JAMA 2009; 301:1439
Study Design

Chronic heart failure, NYHA Class II-IV, LVEF ≤ 35%, optimal medical therapy, and capable of exercising

Pre-randomization CPX and ECHO

Randomization 1:1 (Stratified by center and HF etiology)

Usual Care
- Optimized medical treatment
- Patient education
- Phone calls
  *Recommendation: Moderate intensity activity 30 minutes/day*

Exercise Training
- Optimized medical treatment
- Patient education
- Phone calls
  *Supervised training*
  *Home training*
HF-ACTION Results

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 = .03

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.

JAMA 2009; 301:1439
## Summary of Major Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All-cause mortality and hospitalization (primary)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Main analysis</td>
<td>0.93</td>
<td>0.84, 1.02</td>
<td>0.13</td>
</tr>
<tr>
<td>Adjusted analysis</td>
<td>0.89</td>
<td>0.81, 0.99</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>CV mortality and CV hospitalization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main analysis</td>
<td>0.92</td>
<td>0.83, 1.03</td>
<td>0.14</td>
</tr>
<tr>
<td>Adjusted analysis</td>
<td>0.91</td>
<td>0.82, 1.01</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>CV mortality and HF hospitalization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main analysis</td>
<td>0.87</td>
<td>0.75, 1.00</td>
<td>0.06</td>
</tr>
<tr>
<td>Adjusted analysis</td>
<td>0.85</td>
<td>0.74, 0.99</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Barriers to Utilization of Cardiac Rehabilitation

- Fewer than 20% of all eligible patients participate in a CR
  - Of those who are referred to CR only 34% actually enroll
- Factors contributing to poor utilization
  1) lack of a centralized method for referral
  2) inadequate communication among treatment teams, patients, and CR facilities
  3) unfamiliarity with CR among potential referring physicians
  4) limited access, and perceived inconvenience for the patient (e.g. Copays)
Current Reimbursement for Cardiac Rehabilitation

- With the affordable care act there is a focus on preventive services
- There has been a gradual increase in reimbursement for cardiac rehabilitation
- Currently in California
  - Medicare: $107 per session
  - Commercial Payers (e.g. Anthem Blue Cross): $132 per session
  - For intensive cardiac rehab (ICR), 72 covered sessions
    - revenue is $7700 to $9500 per patient
# Ornish Versus Pritikin

<table>
<thead>
<tr>
<th></th>
<th>Ornish</th>
<th>Pritikin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Number of Sessions covered</strong></td>
<td>72 sessions (divided into 18 sessions that are 4 hours each)</td>
<td>72 sessions (can customize how many sessions per day)</td>
</tr>
<tr>
<td><strong>Diet</strong></td>
<td>100% plant based</td>
<td>Allows for lean meat and fish</td>
</tr>
<tr>
<td><strong>Format</strong></td>
<td>All with live instructors:</td>
<td>Some parts are Video Instruction. Sessions duration can be customized over 18 weeks</td>
</tr>
<tr>
<td></td>
<td>1 hour of exercise</td>
<td></td>
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<tr>
<td></td>
<td>1 hour of nutrition counseling</td>
<td></td>
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<tr>
<td></td>
<td>1 hour of yoga and</td>
<td></td>
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<tr>
<td></td>
<td>1 hour of group therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patients are in groups of 10-12 and stay with the same cohort throughout the program</td>
<td></td>
</tr>
<tr>
<td><strong>Outcome Data</strong></td>
<td>The Lifestyle Heart Trial showed significant regression of coronary atherosclerosis measured by angiography in the experimental group randomly assigned to intensive lifestyle changes. (5 year results reported by Ornish JAMA 1998)</td>
<td>Data from Pritikin residential treatment centers showed improvement in lipids, A1c, blood pressure and weight. (Barnard Am J Cardiol 1992)</td>
</tr>
</tbody>
</table>
Lifestyle Heart Trial

% Diameter Stenosis: Quantitative Coronary Arteriography

Baseline (n.s.) 1y (P.02) 5y (P.001)

Case Study of a Patient from UCLA-Enrolled in ICR

Improvement after only 9 weeks of ICR at UCLA.
New Paradigm For Cardiac Rehabilitation

- “Living Lab” for research and secondary prevention
- Ideal population to deploy new technologies to prevent readmission
  - Good outcome trials needed
- Using devices/wearables to expand the length and scope of cardiac rehabilitation
Beat-HF Trial

1437 hospitalized patients for HF were randomized

Intervention Arm: n=715 patients

Usual Care Arm: n=722 patients

Patients followed for 180 days

No difference in outcomes

Intervention:
- Combined health coaching telephone calls and telemonitoring (BP, HR and weight)
- Centralized registered nurses conducted telemonitoring reviews, protocoted actions, and telephone calls

Scripps Wired for Health Study

160 patients with hypertension, diabetes, or arrhythmia randomized

Intervention Arm: n=75 patients (monitored)

Control Arm: n=85 patients

Patients followed for 6 months

No difference in outcomes or costs
Scripps Wired for Health Study

- Members of the intervention group were issued an iPhone 4 and a connected device:
  - Hypertension: Withings blood pressure monitor
  - Diabetes: Sanofi IBGStar blood glucose
  - Arrhythmia: AliveCor ECG monitor

- Results
  - No difference in outcomes (BP, HBA1c between the groups)
  - No difference in health care costs or utilization as a result of the intervention

PeerJ 4:e1554  https://doi.org/10.7717/peerj.1554
Mayo Clinic Study (Apps + Cardiac Rehab)

- 44 patients
  - 25 in the app + cardiac rehab arm
  - 19 in cardiac rehabilitation without the app arm

- The app tracked and monitored patient weight, BP, blood sugar and physical activity and provided educational content

- The app group had 40% less readmissions and lower blood pressure and weight
From: THE AUGMENTATION OF USUAL CARDIAC REHABILITATION WITH AN ONLINE AND SMARTPHONE-BASED PROGRAM IMPROVES CARDIOVASCULAR RISK FACTORS AND REDUCES REHOSPITALIZATIONS

Primary Results of the HABIT Trial
(Heart Failure Assessment With BNP in the Home)

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Kelly Borden, MD,*† Navaid Iqbal, MD,* Pam R. Taub, MD,*† Ken Kupfer, PhD,‡‡
Paul Clopton, MD,* Barry Greenberg, MD†
San Diego, Loma Linda, Banning, Orange, Mission Viejo, Irvine and Rancho Mirage, California

Objectives
This study was a multicenter, single-arm, double-blinded observational prospective clinical trial designed to mon-
tor daily concentrations of B-type natriuretic peptide (BNP) and to determine how these concentrations correlate
with acute clinical heart failure decompensation (ADHF) and related adverse clinical outcomes in at-risk HF
patients.

Background
Although BNP at discharge is predictive of 30-day outcomes, outpatient serial testing may improve the risk of
detecting early decompensation.

Methods
A total of 163 patients with HF signs and symptoms of ADHF discharged from the hospital or in an outpatient
setting measured their weight and BNP levels daily for 60 days with a finger-stick test. Patients and physicians
were blinded to BNP levels. The composite outcome was ADHF events: cardiovascular death, admission for de-
compensated HF, or clinical HF decompensation requiring either parenteral HF therapy or changes in oral HF
medications.

Results
A total of 6,934 daily BNP values were recorded, with a median of 46 measures per patient over a monitoring
period of 65 days. Forty patients had 56 events. Correlations between BNP measures weakened over time, and
the dispersion between BNP measures grew. During 10,035 patient-days, there were 494 (4.9%) days of weight
gain (≥5 lbs). The hazard ratio per unit increase of In BNP was 1.84, and the hazard ratio on a day of weight
gain was 3.63. These effects retained significance when controlling for symptoms. When the monitoring period
for each subject was broken into intervals based on ADHF events, there were 39 (18.4%) intervals of upward
trending BNP corresponding to a risk increase of 59.8% and 64 (30.2%) downward trending intervals corre-
sponding to a risk decrease of 39.0%. There were 94 (44.3%) intervals with 1 or more days of weight gain corre-
sponding to a risk increase of 26.1%.

Conclusions
This pilot study demonstrates that home BNP testing is feasible and that trials using home monitoring for guid-
ing therapy are justifiable in high-risk patients. Daily weight monitoring is complementary to BNP, but BNP
changes correspond to larger changes in risk, both upward and downward. (Heart Failure [HF] Assessment with
B-type Natriuretic Peptide [BNP] In the Home [HABIT]; NCT00946231) (J Am Coll Cardiol 2013;61:1726–35)
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Exercise Training for POTS

- Physical deconditioning (i.e., low stroke volume and reduced LV mass) and reduced standing stroke volume may be important to the pathophysiology of POTS

- Physical reconditioning with short-term exercise training significantly increased:
  - peak oxygen uptake,
  - expanded blood and plasma volume,
  - improved POTS orthostatic intolerance symptoms,
  - and in most cases allowed these patients to be symptom free
### Study of Exercise in POTS

**Table 2** Short-term exercise training program

<table>
<thead>
<tr>
<th>Training type</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base pace (RPE 13–15)</td>
<td>10 × 30 min</td>
<td>6 × 30 min</td>
<td>5 × 35 min</td>
</tr>
<tr>
<td>Maximal steady state (RPE 16–18)</td>
<td>1 × 20 min</td>
<td>1 × 25 min</td>
<td>1 × 30 min</td>
</tr>
<tr>
<td>Maximal steady state (RPE 16–18)</td>
<td>1 × 25 min</td>
<td>1 × 30 min</td>
<td>1 × 35 min</td>
</tr>
<tr>
<td>Recovery (RPE 6–12)</td>
<td>2 × 40 min</td>
<td>1 × 40 min</td>
<td>3 × 25 min</td>
</tr>
<tr>
<td>Strength training</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular modes</td>
<td>8 × 15–20 min</td>
<td>8 × 20–25 min</td>
<td>8 × 30 min</td>
</tr>
<tr>
<td>Recumbent bike</td>
<td>Swimming</td>
<td>Month 1 modes plus</td>
<td>Month 1 and 2 modes plus</td>
</tr>
<tr>
<td>Rowing</td>
<td></td>
<td>upright bike</td>
<td>elliptical and treadmill</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>walking</td>
</tr>
</tbody>
</table>

RPE = rating of perceived exertion (subjective rating of the entire cardio workout on a scale of 6–20: 6 is very, very easy; 11 is fairly easy; 13 is somewhat hard; 15 is hard; 17 is very hard; 19 is very, very hard).

- 103 patients completed the exercise program
**Exercise Training for POTS**

- **HR (beats/min)**
  - Before training: 
  - After training: 
  - *P* < 0.001 for posture
  - *P* < 0.001 for training
  - *P* < 0.001 for interaction

- **Δ HR (beats/min)**
  - Before: 
  - After: 
  - *P* < 0.001

- **SBP (mmHg)**
  - Supine: 
  - 1 min, 3 min, 5 min, 10 min: 
  - *P* = 0.080 for posture
  - *P* = 0.759 for training
  - *P* = 0.391 for interaction

- **DBP (mmHg)**
  - Supine: 
  - 1 min, 3 min, 5 min, 10 min: 
  - *P* < 0.001 for posture
  - *P* = 0.220 for training
  - *P* = 0.047 for interaction
Exercise Training in PAD

The magnitude of functional benefit derived from exercise training exceeds that observed in drug therapy trials with both pentoxifylline and cilostazol (Circulation. 2011;123:87-97)

<table>
<thead>
<tr>
<th>Table 2. Exercise Prescription for Supervised Endurance Training in PAD Patients With Intermittent Claudication</th>
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<tbody>
<tr>
<td><strong>Frequency</strong></td>
</tr>
<tr>
<td><strong>Modality</strong></td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
</tr>
<tr>
<td><strong>Duration</strong></td>
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<tr>
<td>Pathophysiological Process</td>
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<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Arterial obstruction</td>
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<tr>
<td>Endothelial dysfunction</td>
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<tr>
<td>Mitochondrial dysfunction</td>
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<tr>
<td>Inflammatory activation</td>
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</table>
Conclusions

- New era in cardiac rehabilitation ushered in by change in focus and reimbursement of our health care system
- Appropriate use of cardiac rehabilitation can lead to improved outcomes
- Expansion of cardiac rehabilitation to diseases such as HFPEF and POTS in the future
- Many digital health devices/apps but need good outcome data