Cardiac Rehabilitation: When, How (and Why)
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Optimal Medical Therapy (OMT) for CAD

Management Interventions Which Reduce Secondary Cardiac Events/Death:
- Revascularization (PCI/CABG)
- ASA
- Beta-blockers
- Statin Dyslipidemia Treatment
- ACE
- Exercise
- Nutrition and PUFAs
- Stress Management

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Exercise is Superior to PCI: 101 men with stable symptomatic CAD randomized to regular exercise vs PCI and followed for 12 months.

No benefit of initial stent vs. medical therapy for stable CAD

Meta-analysis of Randomized Controlled Trials
- 8 trials conducted between 1997-2005 that enrolled 7,229 patients
- Conclusion: Support current recommendations for instituting optimal medical therapy (OMT) in patients with stable CAD rather than proceeding directly to stent implantation

Meta-analysis, Circulation 2004

DISCLOSURE INFORMATION:
The following relationships exist related to this presentation (*paid to CSMC):
- Grant support*: NHLBI, SWHR, Gilead
- Consulting*: Abbott Vascular, Amarin, Pozen, Medscape, BMS
- Honorarium*: Gilead, Allegheny, Brigham and Women’s, CV Institute San Diego, El Camino Hosp, Expert Exchange, Mayo, Montefiore, SCS, Slocum-Dickson, Women’s Health Congress, Los Robles Med Ctr, U Penn
- Stocks: None
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**Synergistic effect of statins and exercise on mortality risk in dyslipidemia**

- Combining treatment with statins with better physical fitness can boost survival in patients with dyslipidemia
- Highly fit on statins had 70% reduction in mortality compared with unfit

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**Nutrition**

- **Mediterranean nutrition** 4 RCT +++
- **Fish Intake** 1.5 RCT ++
- **Fish Oil Supplements** 20 RCT -

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**Statins and Exercise: Additional Benefit**

- **LDL-C Levels and Event Rates in Secondary Prevention Trials of Patients with Stable CHD**

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**Relationship between LDL Levels and Event Rates in Secondary Prevention Trials of Patients with Stable CHD**

- **HMG-CoA Reductase Inhibitor: Secondary Prevention:**
  - Overall 30-40% risk reduction

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**Kokkinos PF, Lancet 2012; Available online 27 November 2012**

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### USDA vs. Mediterranean Dietary Recommendations

- **USDA Pyramid**
  - Vegetables, fruits, whole grains, legumes, and nuts
  - Grains, fats, and sweet others

- **Mediterranean Pyramid**
  - Olive oil, fish, vegetables, and beans
  - Lean meats, dairy, and whole grains

### Comparison of the Diets (Lyon Trial)

<table>
<thead>
<tr>
<th>Item</th>
<th>Experimental</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total calories</td>
<td>1947</td>
<td>2088*</td>
</tr>
<tr>
<td>Total fat</td>
<td>30.4%</td>
<td>33.6%*</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>8%</td>
<td>11.7%</td>
</tr>
<tr>
<td>Dietary cholesterol</td>
<td>203 mg/dl</td>
<td>312 mg/dl*</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Same</td>
<td>Same</td>
</tr>
<tr>
<td>Olive oil</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>MUFA n-9</td>
<td>Increased*</td>
<td></td>
</tr>
<tr>
<td>PUFA</td>
<td>Increased*</td>
<td></td>
</tr>
<tr>
<td>n-3/n-6 fatty acids</td>
<td>Increased*</td>
<td></td>
</tr>
<tr>
<td>Fiber</td>
<td>18.6</td>
<td></td>
</tr>
</tbody>
</table>

*Significantly different


### Diet Evidence: Secondary Prevention

- **A Mediterranean diet reduces CVD event rates**
  - 60% patients following a MI randomized to a Mediterranean or Western diet for 4 years

### The JAMA Network

**Figure Legend:**

- **Diet and Reinfarction Trial (DART)**
  - Gruppo Italiano per lo Studio della Sopravvenienza nell’Infarto miocardico (GISSI)

- **ω-3 Fatty Acids: Secondary Prevention**
  - N-3 Fatty Acids: Secondary Prevention
  - DART (n=3,482) GISSI (n=11,324)
  - ω-3 fatty acids reduce mortality post MI


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From: Effect of a Mediterranean Diet Supplemented With Nuts on Metabolic Syndrome Status: One-Year Results of the PREDIMED Randomized Trial


Odds ratios (ORs) and 95% confidence intervals (CIs) of 1-year reversion among participants who had the metabolic syndrome (MetS) at baseline (top) and incidence among participants who did not have MetS at baseline (bottom) in the 2 Mediterranean diet (MedDiet) groups compared with the control diet group. The logistic regression model was adjusted for sex, age, baseline obesity status, and weight changes. CVD indicates cardiovascular disease; DART, Diet and Reinfarction Trial; GISSI, Gruppo Italiano per lo Studio della Sopravvenienza nell’Infarto miocardico; N-3 fatty acids, ω-3 fatty acids; OR, odds ratio; VOO, virgin olive oil.
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M-HART: A Randomized Trial of Psychosocial Stress Intervention following MI

<table>
<thead>
<tr>
<th>Stress Intervention</th>
<th>Overall (n=1376)</th>
<th>Men (n=903)</th>
<th>Women (n=473)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>1.4 (0.85-2.29)</td>
<td>0.97 (0.46-2.03)</td>
<td>1.94 (0.99-3.8)</td>
</tr>
<tr>
<td></td>
<td>p=0.18</td>
<td>p=0.93</td>
<td>p=0.055</td>
</tr>
</tbody>
</table>

Frasure-Smith et al, JACC 1997;452A

Exercise, CHD and Depression: UPBEAT Study

- Understanding the Prognostic Benefits of Exercise and Antidepressant Therapy (UPBEAT) study included 101 patients with CHD and elevated depressive symptoms
- 4 months of aerobic exercise three times per week; 50 mg to 200 mg of sertraline (Zoloft, Pfizer) daily; or placebo.
- Increased physical activity decreased depressive symptoms in clinically depressed patients with CHD

Blumenthal JA et al. J Am Coll Cardiol. 2012;60(12):1053-1063

Exercise 3 times per week significantly greater reduction in depressive scores
Meditation - Trial Design

- Randomized, controlled, single-blinded intervention study
- 103 stable CHD patients
- Rolling enrollment over 2.5 years from 1/1/2000-6/1/2002
- Randomization stratified according to age, LDL-C and Reproductive Hormone Replacement Therapy use
- 16 weeks of either TM or Health Education
- Both groups have similar duration and frequency of instruction
- Both groups practice daily for two 20 minute sessions

Adjusted Change (Exit-Entry) in HRV*

<table>
<thead>
<tr>
<th></th>
<th>(N=43)</th>
<th>(N=35)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>△ Total Power</td>
<td>-0.01 ± 0.18</td>
<td>-0.49 ± 0.19</td>
<td>0.092</td>
</tr>
<tr>
<td>△ High Frequency Power</td>
<td>0.10 ± 0.17</td>
<td>-0.50 ± 0.17</td>
<td>0.023</td>
</tr>
<tr>
<td>△ Low Frequency Power</td>
<td>-0.01 ± 0.18</td>
<td>-0.47 ± 0.18</td>
<td>0.091</td>
</tr>
</tbody>
</table>

*adjusted for age, gender, baseline HRV variable, BMI at exit, physical activity level, history of MI, depression score at baseline, anger score at baseline.
Paul-Labrador et al, Archives Int Med 2009

A Randomized Controlled Trial of Transcendental Meditation in the Treatment of Coronary Heart Disease

Acupuncture - Trial Design

- Randomized, controlled, single-blinded intervention study
- 135 stable CHD patients
- 12 weeks of either TA or SA three times weekly.
- Waiting control gets 4 weeks free TA at end.
- SA placed at points close to TA points, but needle not inserted.
- Pilot Study: SA named “Alternative Acupuncture” and validated to be indistinguishable from TA

Acupuncture Points
HRV Results

<table>
<thead>
<tr>
<th>Time Domain</th>
<th>TA (n = 38) Mean ± SD</th>
<th>SA (n = 43) Mean ± SD</th>
<th>P-value (TA vs. SA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LF</td>
<td>6.09 ± 1.44</td>
<td>5.63 ± 0.97</td>
<td>0.100</td>
</tr>
<tr>
<td>HF</td>
<td>5.21 ± 1.41</td>
<td>4.89 ± 1.06</td>
<td>0.068</td>
</tr>
<tr>
<td>LF/HF</td>
<td>1.18 ± 0.18</td>
<td>1.28 ± 0.24</td>
<td>0.018</td>
</tr>
<tr>
<td>TF</td>
<td>7.84 ± 1.24</td>
<td>7.02 ± 0.81</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Frequency Domain

- Mean NN: 1026 ± 186, 965 ± 115, 0.021
- SDNN: 77.54 ± 43.8, 59.31 ± 28.7, 0.033
- SDANN: 92.70 ± 25.4, 24.12 ± 21.8, 0.936
- rSDNN: 450.14 ± 41.79, 449.29 ± 20.9, 0.970
- RMSSD: 28.30 ± 20.6, 24.21 ± 11.7, 0.019
- pNN50: 15.26 ± 15.9, 5.66 ± 8.5, 0.002

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Exercise Evidence: Mortality Risk: 25-35% Risk Reduction

Observational study of self-reported physical activity in 772 men with established coronary heart disease

- Light or moderate exercise is associated with lower risk

Mechanisms of Cardiac Rehabilitative Benefit

- Reduction of Insulin Resistance/Diabetes
- Reduction of Vascular Inflammation
- Improved Hemodynamics Contributing to ACS, MI and HF
- Compliance with OMT

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Probability of CHD death in diabetic and nondiabetic people with and without MI

Graph showing survival percentages for different conditions and groups.
Physical Activity and Mortality in Individuals With Diabetes Mellitus
A Prospective Study and Meta-analysis

40% Risk Reduction

Mechanisms of Cardiac Rehabilitative Benefit
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Leisure-time activity and inflammatory markers
Middle-aged adults who engaged in regular leisure-time physical activity for more than a decade had lower markers of inflammation and enhanced CV health
Leisure-time physical activities, including brisk walking, gardening, cycling, sports, housework and home maintenance
BOTTOM LINE: becoming active in mid-life can still have benefits for CV health since participants in this study were all aged 50 to 60 years

Leisure-time activity and inflammatory markers

Hamer M. Circulation 2012 Aug 21;126(8):928-33

Exercise Physiology
Cardiovascular Effects of 1 Year of Progressive and Vigorous Exercise Training in Previously Sedentary Individuals Older Than 65 Years of Age

Hamer M. Circulation 2012 Aug 21;126(8):928-33
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Cardiac Rehabilitation: Who, When (and Why)

- 1. Cardiac rehabilitation/exercise/nutrition intervention is superior to revascularization and additive to statin optimal medical therapy (OMT) for secondary prevention of CVD.
- 2. Mechanistic pathways include reduction of insulin resistance/diabetes, inflammation and hemodynamic dysfunction and compliance with OMT.
- 3. Cardiac rehabilitation is under-utilized in the US.
- 4. Improved cardiac rehabilitation reimbursement and healthcare reform in the US is aimed at improving secondary prevention of CVD.