Evidence for Incorporating Aerobic Exercise into Stroke Recovery

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  - Career development award
“If exercise could be purchased in a pill, it would be the single most widely prescribed and beneficial medicine in the nation.”

- Robert H. Butler
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- Robert H. Butler
• How often do we tell our patients to take their exercise “medicine”
• How much of this “medicine” do we prescribe?
• How many times per day should the “medicine” be taken?
• What type of “medicine”? 
• F.I.T.T Principle
Moving Forward

• Implement more evidence-based approach:
  – Screen to ensure safety for aerobic exercise
  – Exercise testing
    • Maximal
    • Submaximal
  – Exercise prescription
  – Monitor safety
Physical Activity and Exercise Recommendations for Stroke Survivors: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

Sandra A. Billinger, Ross Arena, Julie Bernhardt, Janice J. Eng, Barry A. Franklin, Cheryl Mortag Johnson, Marilyn MacKay-Lyons, Richard F. Macko, Gillian E. Mead, Elliot J. Roth, Marianne Shaughnessy and Ada Tang

on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Lifestyle and Cardiometabolic Health, Council on Epidemiology and Prevention, and Council on Clinical Cardiology

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• Activity intensity is low in rehabilitation and declines further in the first year post-stroke (Bernhardt, 2007; Reisman, 2012)

• Aerobic component is near-zero in practice (MacKay-Lyons, 2002)

• We need to monitor intensity in rehabilitation and home
  – Heart rate, repetitions, perceived exertion

• Consider innovative methods to increase intensity in rehab
• Observable study\(^1\) (Australia)
  – Time spent physically active or inactive
  – Within first 2 weeks following stroke
    • Patients resting in bed 53% of time
    • PT/OT/SLP combined to only 5.2%
    • 84.5% had no precautions or bed rest orders
    • Patients with very mild stroke
      – Spent mere 11% of day doing standing activity
      – Independent walkers: 40.5% sedentary
      – Bed bound patients: 98% sedentary
Lower Extremity Accelerometry and Stroke

• Chronic stroke (United States)
  – Use of accelerometers (3 days)
  – Older adults vs people post-stroke
  – Bouts of activity shorter in people post-stroke
  – Limits cardiovascular benefits

• Subacute stroke (n = 8) (Canada)
  – Use of accelerometers during in-patient rehab
  – Measure HR and activity for 8 hours for one day
  – Walking intensity < 40% HRR; Duration < 10 min
Physical Activity Levels in Acute Stroke (PALAS)

- Enroll stroke patients 24 hours post-stroke
  - Functional testing
    - Physical Performance Test
    - Timed Up and Go
    - 6-MWT
  - Baseline and at discharge
- Accelerometer data
  - Wear 24 hours/day
- Multidisciplinary efforts
  - Social work, nursing, rehab, research team, stroke neurologists/residents
<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Admission to KU Hospital with diagnosis of stroke</td>
<td>• Physician ordered bed-rest</td>
</tr>
<tr>
<td>• Between the age of 20 and 80 years</td>
<td></td>
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<tr>
<td>• Able to obtain consent within 48 hours of admission</td>
<td></td>
</tr>
</tbody>
</table>
Physical Activity Levels in Acute Stroke (PALAS)

• Enrolled 38 stroke patients 24 hours post-stroke
  – Functional testing
    • Physical Performance Test
    • Timed Up and Go
    • 6-MWT
  – Baseline and at discharge

• Accelerometer data
  – Wear 24 hours/day

• Multidisciplinary efforts
  – Social work, nursing, rehab, research team, stroke neurologists/residents
PALAS Results

• Sample size of n = 32
  – Gender (18 males)
  – Age = 56.5 years ± 12.7 (35-75 years)
  – BMI = 28.3 ± 5.2
  – Non-exercise predicted VO₂ peak = 26.6 ± 8.1
  – LE Fugl-Meyer Score = 25.5/34 ± 9.1
PALAS Results

- Mean time spent:
  - 93.9 (4.1)% Sedentary
  - 5.1 (2.4)% Light Activity
  - 0.7 (0.7)% Moderate Activity
  - 0% Vigorous Activity

- Length of sedentary bouts per day
  - 1354.65 ± 58.6 minutes

- 6MWT distance
  - T1: 152.38 ± 121.8 meters

Healthy older adults (OA): 75% sedentary & 21% light activity (Arnardottir, 2012)

Healthy OA 6MWT: 572 m (men) & 538 m (women) (Steffen, 2002)
Results

• Baseline and post-testing data

• Relationship between:
  – Sedentary bouts per day and functional outcomes at discharge
  – PPT
    • $r = -0.53$, $p < 0.05$

• Walking Performance
  – 6MWT
    • $r = -0.20$, $p = 0.29$
  – TUG ($n = 23$)
    • $r = 0.24$, $p = 0.37$
Take Home Message (PALAS)

• Acute stroke patients are sedentary
  – Hospital environment?
  – Lack of desire to move around?
  – Unsure what to do?
  – Does this translate to in-patient or community living?

• Healthcare team
  – What do we do about this?
Exercise and Stroke Rehabilitation

• Exercise beneficial in chronic stroke survivors
• What does the current literature show early after stroke?
  – AVERT (A Very Early Rehabilitation Trials) (Bernhardt, et al)
  – Robot-assisted gait training (Chang and colleagues, 2012)
    • Enrolled prior to one-month post-stroke
    • Randomized control trial (60 + 40 minutes of traditional PT; 60 minutes PT + 40 minutes robot-gait assist)
Inpatient Rehabilitation

Recumbent cycling in-patient rehabilitation (Tang and colleagues, 2009)

- Enrolled ~ 17.8 (6-62) days post-stroke
- Maximal exercise test
  - Intensity 50-70% work rate
- Recumbent cycle ergometer
- Results
  - Both groups improved in outcome measures but exercise group greatest improvement
    - CR Fitness
    - 6 MWT
    - TUG
Inpatient Rehabilitation

– Body weight supported TM training vs usual care
  (MacKay-Lyons, 2013)
  • 12-week intervention
  • 60 minute of therapy (25-30 minutes; overground or BWSTT)
  • Significant group x time interaction for peak VO2, 6MWT
  • Effects remained at 6 and 12 weeks post-intervention
Inpatient Rehabilitation

Group exercise program by physiotherapist (Bisain and colleagues, 2014)

- Feasibility and aerobic exercise
- Submaximal exercise test
- Recumbent cycle ergometer and recumbent steppers
Results (Biasin and colleagues, 2014)

- 40% were referred to exercise program
  - Cardiac comorbidities
  - 77% attendance of those enrolled
- Physiotherapists conservative with exercise duration and intensity vs results of submaximal exercise test
- Stroke survivors didn’t meet targets for HR range or duration of exercise

Aerobic exercise intervention in subacute stroke (CRESS) (Billinger and colleagues, 2012)

- Cardiopulmonary and vascular function
- Physical performance (walking)
Cardiovascular Regulation, Exercise in Sub-acute Stroke (CRESS) Study

- Goal: Enroll 10 people post-stroke
- 8-week aerobic exercise intervention (3 times per week)
  - Recumbent Stepper
- Exercise Parameters:
  - SBP less than 220 mmHg
  - DBP less than 105 mmHg
  - RPE between 12-16/20
  - Polar HR Monitor
    - HR Reserve
      - 50-59% (First 4 weeks)
      - 60-69% (Second 4 weeks)
- Outcome Measures
  - Pre, post-intervention, one-month follow-up
  - Functional Outcome
    - 6-MWT
  - Cardiorespiratory Health
    - HR, SBP, DBP, VO$_2$ peak, exercise test time, and watts
    - Submax test to predict
  - Vasomotor reactivity (Flow-mediated dilation/reactive hyperemia)
When the blood pressure cuff is released, brachial artery blood flow is immediately higher than its resting level and gradually decreases toward normal levels. Excess blood flow (reactive hyperemia).
## Participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number or Group Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.2 (4.7)</td>
<td>52-70</td>
</tr>
<tr>
<td>Days Post-Stroke</td>
<td>68.6 (40.1)</td>
<td>15-123</td>
</tr>
<tr>
<td>Overall ABI</td>
<td>0.98 (0.11)</td>
<td></td>
</tr>
<tr>
<td>Fugl-Meyer</td>
<td>100.3 (29.3)</td>
<td>35-124</td>
</tr>
<tr>
<td>Regular Exercisers Pre-Stroke</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
# Flow Mediated Dilation

<table>
<thead>
<tr>
<th></th>
<th>Baseline n=9</th>
<th>Post-Intervention n=9</th>
<th>Change %</th>
<th>p-value</th>
<th>1-month follow-up n=7</th>
<th>p-value Baseline to follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMD&lt;sub&gt;affected&lt;/sub&gt; (%)</td>
<td>4.7 (2.5)*</td>
<td>5.4 (2.4)*</td>
<td>18.5</td>
<td>0.001</td>
<td>5.4 (2.5)*</td>
<td>0.05</td>
</tr>
<tr>
<td>FMD&lt;sub&gt;nonaffected&lt;/sub&gt; (%)</td>
<td>6.5 (2.2)</td>
<td>7.7 (2.3)</td>
<td>19.4</td>
<td>0.001</td>
<td>7.1 (2.9)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Data expressed as mean (SD) unless otherwise stated. FMD = flow-mediated dilation; * indicates p <0.02 for between-limb differences at each timepoint (baseline, post-intervention and follow-up)
## Cardiovascular and Physical Performance

<table>
<thead>
<tr>
<th></th>
<th>Baseline n=9</th>
<th>Post-Intervention n=9</th>
<th>p-value</th>
<th>1-month follow-up n=8</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>81.2 (14.1)</td>
<td>78.7 (12.9)</td>
<td>0.25</td>
<td>74.8 (10.1)</td>
<td>0.08</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>134.4 (8.6)</td>
<td>122.4 (11.1)*</td>
<td>0.001</td>
<td>131.4 (12.6)</td>
<td>0.27</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>78.2 (10.2)</td>
<td>76.8 (6.3)</td>
<td>0.34</td>
<td>77.3 (5.5)</td>
<td>0.25</td>
</tr>
<tr>
<td>6 MWT</td>
<td>304.1 (167.5)</td>
<td>342.8 (185.6)</td>
<td>0.002</td>
<td>363.6 (201.2)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Data expressed as mean (SD). HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; RER = respiratory exchange ratio; 6 MWT = Six minute walk test. * indicates significance with p ≤0.02 baseline and 1) post-intervention and 2) 1 month follow-up.
# Peak Exercise Hemodynamic Measures

<table>
<thead>
<tr>
<th></th>
<th>Baseline n=9</th>
<th>Post-Intervention n=9</th>
<th>p-value</th>
<th>1-month follow-up n=8</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>**VO(_2)peak (mL<em>kg(^{-1})<em>min(^{-1}))</em></em></td>
<td>15.8 (3.9)</td>
<td>17.5 (6.2)</td>
<td>0.04</td>
<td>17.4 (7.4)</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>HR (bpm)</strong></td>
<td>142.9 (18.0)</td>
<td>144.2 (20.4)</td>
<td>0.40</td>
<td>143.3 (20.1)</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>RER</strong></td>
<td>1.1 (0.1)</td>
<td>1.1 (0.1)</td>
<td>0.44</td>
<td>1.2 (0.1)</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>RPE</strong></td>
<td>18.9 (1.7)</td>
<td>17.4 (2.8)</td>
<td>0.08</td>
<td>17.4 (2.1) *</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Work (Watts)</strong></td>
<td>66.7 (26.5)</td>
<td>83.3 (32.9)*</td>
<td>0.004</td>
<td>90.6 (33.2) *</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Exercise Time (sec)</strong></td>
<td>654.1 (215.2)</td>
<td>700.9 (212.5)</td>
<td>0.10</td>
<td>707.9 (225.7)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Data expressed as mean (SD). RER = respiratory exchange ratio; RPE = rating of perceived exertion. * indicates significance with p ≤0.02 baseline and 1) post-intervention and 2) 1 month follow-up.

Billinger, et al, JNPT, 2012. (Golden Synapase Award for Best Manuscript)
Summary

• Subacute stroke
  – Limited research supports exercise as beneficial
    • Walking (6MWT)
    • Cardiovascular health
    • Long-term implications for secondary recurrence

• Where do go from here?
  – Acute stroke
  – Vascular health
  – Early Mobility
Medical Clearance/Evaluation

• Consider whether the individual is low, moderate or high cardiac risk
  – High risk may require medical evaluation and determination of exercise supervision

• Exercise prescription
  – May need to monitor:
    • HR or BP limits
    • Blood sugars
    • Orthopedic issues
    • Neurologic deficits

• Baseline for comparison
Risk Stratification Categories for Exercise Testing

Subject ID:

Date:

Please circle any criteria patient has experienced or has a known diagnosis/disease.

Review Health/Medical History for:
- Known Disease
- Signs/Symptoms
- CAD Risk Factors

Known Diagnosis/Disease
- Cardiovascular: Cardiac, peripheral vascular, or cerebrovascular disease
- Pulmonary: COPD, asthma, interstitial lung disease, or cystic fibrosis
- Metabolic: Diabetes mellitus (types 1 and 2), thyroid disorders, renal or liver disease

Known Cardiovascular, Pulmonary, or Metabolic Disease?

Yes

No

Major Signs or Symptoms Suggestive of Cardiovascular, Pulmonary, or Metabolic Disease?

Yes

No

Signs/Symptoms
- Pain, discomfort in the chest, neck, jaw, arms, or other areas that may arise from ischemia
- Shortness of breath at rest or with mild exertion
- Dizziness or syncope
- Orthopnea or paroxysmal nocturnal dyspnea
- Ankle edema
- Palpitations or tachycardia
- Intermittent claudication
- Cough or hemoptysis
- Unusual fatigue or shortness of breath with usual activities

Risk Factors
- Age
- Family History
- Current Opioid Use Disorder
- Sedentary Lifestyle
- Obesity
- Hypertension
- Dyslipidemia
- Pre-diabetes

Number of CAD Risk Factors
- ≥ 2
- ≤ 1

High Risk

Moderate Risk

Low Risk

Low Risk: Asymptomatic men and women who have ≤ 1 CVD risk factor.
Moderate Risk: Asymptomatic men and women who have ≥ 2 risk factors.
High Risk: Individuals who have known cardiovascular, pulmonary, or metabolic disease or one or more symptoms.

*Flowchart modified from ACSM’s Guidelines for Exercise Testing and Prescription 8th Edition, Figure 2.3
Exercise Intensity for Cardiorespiratory (CR) Fitness

• Most challenging task in designing the exercise program
  – Requires **individualization**
  – Monitoring/supervision
• Expressed as a percent of aerobic capacity
  – VO$_2$ max/peak
  – Age adjusted maximum heart rate (AAMHR)
• Monitor intensity during exercise
  – HR, VO$_2$ (via METS), RPE
F.I.T.T Principle and Stroke

• 37 Randomized trials in subacute and chronic stroke (Amman, 2014)

• Lack of consistent reporting on F.I.T.T principle
  – Frequency and type (of modality) = 94.6%
  – Intensity = 59%**
  – Time = 91.9%
Evidence for Why We Should Care

- Improved cardiorespiratory fitness (Macko, 2002; Macko, 2004; Tang, 2009; Billinger, 2012; Marzolini, 2014)
- Walking endurance (Tang, 2009; Billinger, 2012; Marzolini, 2014)
- Cardiovascular risk factors (Prior, 2011)
- Vascular health (Billinger, 2012)
- Cognition (Quaney, 2009; Kluding, 2011)
Exercise and Brain Health

- Aerobic exercise and biomarkers
  - BDNF
  - VEGF
  - IGF-1
- Implications for stroke recovery (Mang, 2013; Mang, 2014)
  - High intensity
  - High intensity interval training
- Dose response for stroke recovery
Cerebrovascular Measures at Rest

- EKG Signal
- MAP Signal
- TCD Signal

Data Point: 1 162 323 484 645 806 967 1128 1289 1450 1611 1772 1933 2094 2255 2416 2577 2738 2899 3060 3221 3382 3543 3704 3865 4026 4187 4348 4509 4670 4831

Potential (Volts): 0.00 1.00 2.00 3.00 4.00 5.00 6.00
Cerebrovascular Measures during Moderate-Intensity Exercise
Summary

• Healthcare professionals need to consider cardiorespiratory fitness and training

• Evaluate and prescribe exercise
  – Evidence-based methods

• Powerful medication
  – Improves
    • Cardiorespiratory fitness
    • Vascular health (risk factors)
    • Brain health
Thank you

- American Heart Association
- Members of the KC Stroke Rehabilitation Conference
- REACH laboratory
  - PhD Students
    - Anna Mattlage
    - Jason-Flor Sisante
    - Abdulfattah Alqahtani
  - DPT students
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