

Ambulatory Rehabilitation - PAH

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Pulmonary Arterial Hypertension

- Progressive obliteration of pulmonary vessels
- Cardiac manifestations
 - Dyspnea
 - Chest pain
 - Syncope
- Several specific medications now approved

Physical Activity in PAH?

“Physical activity should be limited.”
Gaine SP, Rubin LJ. Lancet 1998

EHS Guideline 2004

- It is unclear whether physical activity may have a negative impact on the evolution of PAH. However, potentially hazardous symptoms like severe dyspnoea, syncope and chest pain should be clearly avoided. Exercise should be limited to a symptom-free level in order to maintain adequate skeletal muscles conditioning. Physical activity after meals or in extreme temperatures should be avoided.

ACCP Guideline 2004

We've been here before...

Post-Myocardial Infarction



1950 – Three weeks in bed



2009 – Start rehabilitation soon

Pulmonary Rehabilitation

- Established adjunct to medical therapy in chronic respiratory disease
- Most research on COPD patients:
 - Improves exercise capacity
 - Improves quality of life
 - Reduces admissions to hospital
 - Cost-effective

Pulmonary Rehabilitation

- Multi-modal therapy:
 - Aerobic training
 - Resistance training
 - Motivation
 - Education
 - Nutrition

What is known for PAH?

Exercise Physiology

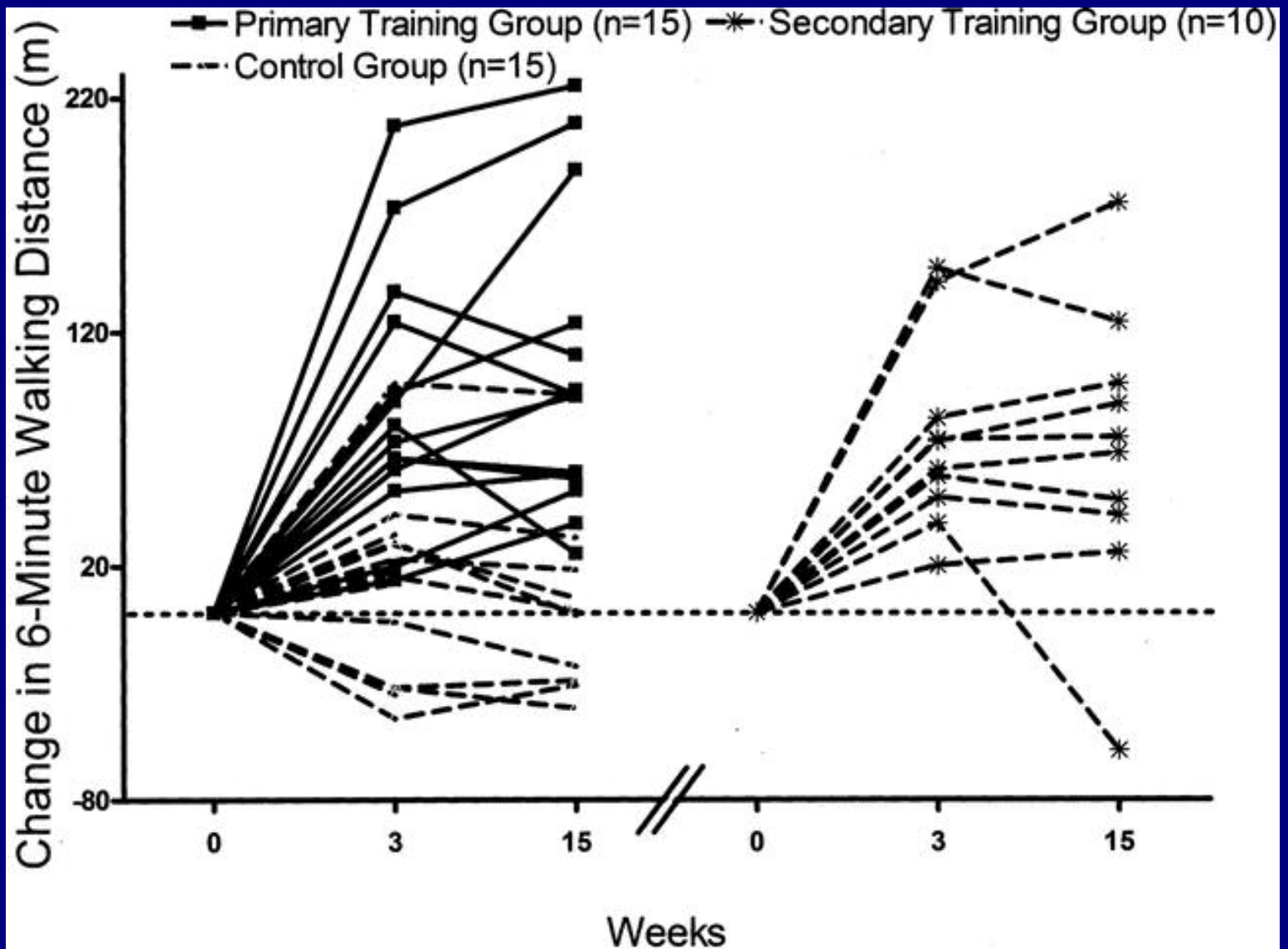
Exercise and Respiratory Training Improve Exercise Capacity and Quality of Life in Patients With Severe Chronic Pulmonary Hypertension

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Mereles et al. 2006

- One single center RCT in Germany
- 30 patients randomized
- 3 weeks in-patient, 12 weeks out-patient
- Control group:
 - Yoga, breathing exercises, massage, motivational talks
- Rehabilitation group:
 - As control group, plus
 - Intensive in-patient rehabilitation
 - 12 weeks home rehabilitation

Rehabilitation - Six minute walk

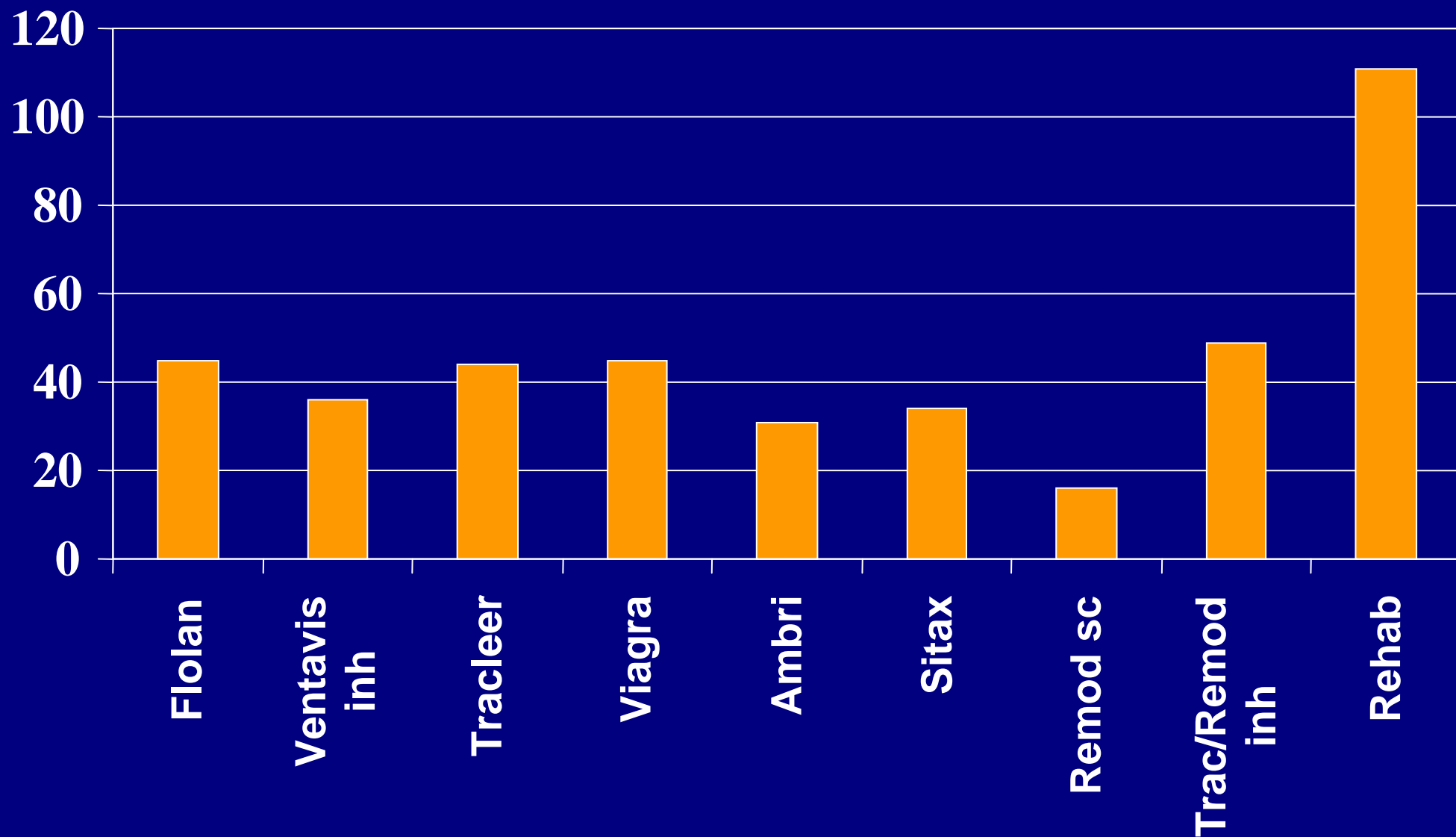


Endpoints

- 6MW
 - Exercise training +96m, Control -15m
- CPET
 - Exercise group increased VO₂, Work rate, AT
- Exercise Echo:
 - No change in PA pressure/peak cardiac output
- No adverse events

Rehabilitation in perspective

Change in 6 minute walk



However

- In-patient rehabilitation extremely expensive
- Not funded by most HMOs outside Germany

Beilinson Study

- Controlled study of ambulatory pulmonary rehabilitation
- Patients with PAH, stable on medication

Open non-randomized study

- Inclusion

- PAH per RHC
- Idiopathic or PAH-associated conditions or chronic pulmonary thromboembolic disease
- Clinically stable on PAH-specific medication 3 months
- NYHA class II-III

- Exclusion

- PAH w/ Eisenmenger, left heart disease, chronic hypoxemia/lung diseases
- Hospital admission in past month
- Significant non-PAH disease
- Recent rehabilitation within 6 months

Assessment

- 6 minute walk (6MW)
- Cardiopulmonary Exercise Test (CPET)
- NT-proBNP
- Echocardiography
- Safety

Endpoints

- Primary:
 - Change in 6MW and VO₂ peak
- Secondary:
 - Other CPET parameters
 - BNP
 - Echo SPAP

Rehabilitation Program

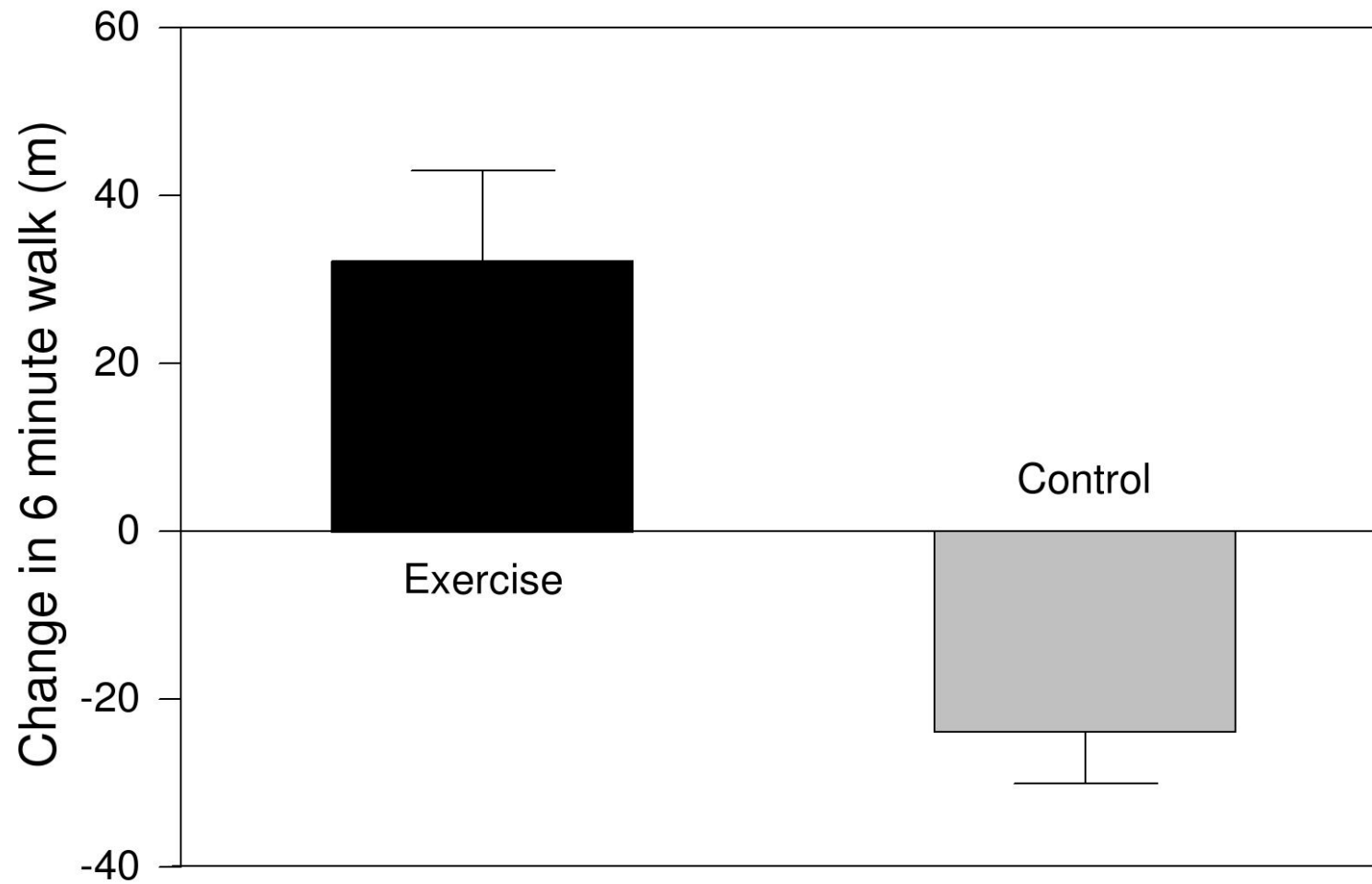
- 12 weeks, two sessions per week
- Patients exercised as a group
- Oxygen provided
- Aerobic and resistance training by an experienced physiotherapist

| | Control | Rehabilitation | p value |
|---------------------------------|------------|----------------|---------|
| Patients (n) | 11 (6M/5F) | 11 (1M/10F) | 0.063 |
| Age (Years) | 46 ± 4.5 | 57 ± 3.7 | 0.14 |
| Weight (kg) | 65 ± 9.4 | 74 ± 6.5 | 0.49 |
| Systolic BP (mmHg) | 115 ± 4 | 111 ± 4 | 0.59 |
| Diastolic BP (mmHg) | 75 ± 4 | 68 ± 3 | 0.36 |
| Hemoglobin (g/dl) | 13.0 ± 0.9 | 12.5 ± 0.7 | 0.65 |
| PAH Diagnosis (n): | ... | ... | 0.167 |
| Idiopathic | 7 | 3 | ... |
| Connective Tissue Disease | 4 | 5 | ... |
| Congenital Heart Disease | 0 | 1 | ... |
| Chronic Thromboembolic | 0 | 2 | ... |
| Treatment: | ... | ... | ... |
| PDE5 Inhibitor | 6 | 4 | 0.67 |
| Endothelin Antagonists | 7 | 7 | 1.0 |
| Prostanoids | 5 | 3 | 0.65 |
| Monotherapy | 4 | 8 | 0.11 |
| Combination Therapy | 7 | 3 | ... |
| Cardiac Catheterization: | ... | ... | ... |
| mPAP (mmHg) | 45 ± 5 | 57 ± 6 | 0.6522 |
| CI (liters/min/m ²) | 3.4 ± 0.9 | 2.03 ± 0.25 | 0.09 |
| PVR (Wood Units) | 11.8 ± 3.1 | 13.5 ± 1.7 | 0.33 |
| RAP (mmHg) | 8 ± 2 | 8 ± 1 | 0.702 |

Results – Primary Endpoints

- 6MW
 - Exercise +32m (11)
 - Control -24m (6)
- p=0.002
- Peak VO₂ (ml/kg/min)
 - Exercise +1.1 (0.3)
 - Control -0.8 (0.3)
- p=0.02

6 minute walk



Results – Secondary Endpoints

- Increase in work rate +14W vs -3W
- No change in AT
- No change in BNP
- No change in Echo

Safety Issues

- No adverse events during training sessions
- SAEs
 - Rehab: One admission for anemia
 - Control: One clinical worsening, one NSCLC

Why did patients improve?

- Cardiac?
- Pulmonary?
- Peripheral?

Limitations

- Small sample
- Non-randomized

Conclusions

- Ambulatory rehabilitation is safe and efficacious to improve exercise capacity in patients with PAH
- Adjunctive therapy to medical Rx

Thank you

Easy questions only please