

## Publikationen

### Dr. med. Robert Nechwatal

1) Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial

Nicola Ehlken · Mona Lichtblau · Hans Klose · Johannes Weidenhammer · Christine Fischer · **Robert Nechwatal** · Sören Uiker · Michael Halank · Karen Olsson · Werner Seeger · Henning Gall · Stephan Rosenkranz · Heinrike Wilkens · Dirk Mertens · Hans-Jürgen Seyfarth · Christian Opitz · Silvia Ulrich · Benjamin Egenlauf · Ekkehard Grünig  
European Heart Journal 07/2015; DOI:10.1093/eurheartj/ehv337 • 15.20 Impact Factor

**ABSTRACT:** The impact of exercise training on the right heart and pulmonary circulation has not yet been invasively assessed in patients with pulmonary hypertension (PH) and right heart failure. This prospective randomized controlled study investigates the effects of exercise training on peak  $VO_2/kg$ , haemodynamics, and further clinically relevant parameters in PH patients. Eighty-seven patients with pulmonary arterial hypertension and inoperable chronic thrombo-embolic PH (54% female,  $56 \pm 15$  years, 84% World Health Organization functional class III/IV, 53% combination therapy) on stable disease-targeted medication were randomly assigned to a control and training group. Medication remained unchanged during the study period. Non-invasive assessments and right heart catheterization at rest and during exercise were performed at baseline and after 15 weeks. Primary endpoint was the change in peak  $VO_2/kg$ . Secondary endpoints included changes in haemodynamics. For missing data, multiple imputation and responder analyses were performed. The study results showed a significant improvement of peak  $VO_2/kg$  in the training group (difference from baseline to 15 weeks: training  $+3.1 \pm 2.7$  mL/min/kg equals  $+24.3\%$  vs. control  $-0.2 \pm 2.3$  mL/min/kg equals  $+0.9\%$ ,  $P < 0.001$ ). Cardiac index (CI) at rest and during exercise, mean pulmonary arterial pressure, pulmonary vascular resistance, 6 min walking distance, quality of life, and exercise capacity significantly improved by exercise training. Low-dose exercise training at 4-7 days/week significantly improved peak  $VO_2/kg$ , haemodynamics, and further clinically relevant parameters. The improvements of CI at rest and during exercise indicate that exercise training may improve the right ventricular function. Further, large multicentre trials are necessary to confirm these results. © The Author 2015. Published by Oxford University Press on behalf of the European Society of Cardiology.

2.) Economic Evaluation of Exercise Training in Patients with Pulmonary Hypertension

Nicola Ehlken · Cora Verduyn · Henning Tiede · Gerd Staehler · Gabriele Karger · **Robert Nechwatal** · Christian F Opitz · Hans Klose · Heinrike Wilkens · Stephan Rosenkranz · Michael Halank · Ekkehard Grünig  
Beiträge zur Klinik der Tuberkulose 03/2014; 192(3). DOI:10.1007/s00408-014-9558-9 • 2.27 Impact Factor

**ABSTRACT:** Exercise training as an add-on to medical therapy has been shown to improve exercise capacity, quality of life, and possibly prognosis in patients with pulmonary hypertension (PH). The purpose of this study was to analyze the impact of exercise training on healthcare costs in PH. Estimated healthcare costs have been compared between patients with severe PH under optimized medical therapy only (control group) versus patients who received exercise training as an add-on to medical therapy (training group). Cost-analysis included a cost-estimation model of costs for baseline and follow-up visits and all PH-related healthcare events that occurred within the follow-up period. Time to clinical worsening and survival were assessed by clinical records, phone, and/or control visits. At baseline, the training (n = 58) and control group (n = 48) did not differ in age, gender, WHO-functional class, 6-min walking distance, hemodynamic parameters, or PH-targeted medication. During a follow-up of 24 ± 12 months, the training group had significantly better survival rates at 1 and 3 years and less worsening events (death, lung transplantation, hospitalization due to PH, new PAH-targeted medication) than the control group (15 vs. 25 events, p < 0.05), which also led to lower estimated healthcare costs of 657 within a period of 2 years. This is the first study to investigate the cost-effectiveness of exercise training in PH. Due to less worsening events within 2 years, healthcare costs were lower in patients performing exercise training as add-on to medical therapy than in patients with medical treatment only. Further prospective, randomized studies are needed to confirm these findings.

### 3) Heidelberger Kompetenztraining (HKT) als Mentaltraining für nachhaltige Effekte in der kardiologischen Rehabilitation

**Robert Nechwatal** · M. Pedak · A. Dillenburger · L. Glatz · I. Haas · K. Moser · W. Knoerzer  
Frühjahrstagung Deutsche Gesellschaft für Kardiologie 2013, Mannheim; 04/2013

**ABSTRACT:** Einleitung: Das Heidelberger Kompetenztraining (HKT) zur Entwicklung mentaler Stärke ist ein psychoedukatives Verfahren, das Strategien vermittelt um individuelle Ziele besser zu erreichen. Wir setzten das HKT innerhalb einer Pilotstudie mit KHK Patienten bei der kardiologischen Rehabilitation zur nachhaltigen Erreichung von Rehazielen ein. Methoden: Das HKT ist aus 4 Schritten aufgebaut: Formulierung von Zielen, Methoden der Konzentration, eigene Stärken aktivieren und mentale Abschirmung. Während der Rehabilitation wurde das HKT 6 Stunden durch erfahrende Kompetenztrainer durchgeführt. Ziel war der Aufbau eines gesunden Lebensstils durch körperliches Training, Ernährungsschulung und Risikofaktorenaufklärung. In der HKT-Gruppe wurden 24 Patienten eingeschlossen (Alter 52,4±7,5 Jahre, EF 60,1 ±8,5%) und in die Kontrollgruppe 21 Patienten (Alter: 52,1±5,8 Jahre, EF 55,9±7 %). Die Kontrollgruppe erhielt alle aktiven und passiven Therapien während der Rehabilitation mit Ausnahme von HKT. Messparameter (6 Minuten-Gehtest, Körpergewicht, Cholesterin und LDL) wurden bei Aufnahme und Entlassung sowie bei Nachkontrollen nach 3 und 9 Monaten erhoben. Jeweils 11 Patienten in jeder Gruppe kamen zum Zeitpunkt 9 nicht zur Nachkontrolle (drop-outs). Ergebnisse: §: p<0,001, & p<0,01, \*: p<,0,05 versus Aufnahme Zusammenfassung: Während der 3 wöchigen stationären Rehabilitation verbesserten sich 6- Minuten Gehtest, Cholesterin und LDI hochsignifikant in der HKT Gruppe: Dieser Effekt hielt über 9 Monate an. In der Kontrollgruppe zeigten sich nur für das LDL signifikante Verbesserungen, die über 3 Monate anhielten.

### 4) Improvement in Autonomic Dysfunction Manifested by Altered Heart Rate Variability, T-Wave Alternans and Norepinephrine by Long Term Exercise in Chronic Heart Failure.

**Robert Nechwatal**, Michael Horn, Uwe Scharf, Bettina Mochalski, Ulrike Lachenmeyer  
Journal of the American College of Cardiology 2004, Suppl, 229-230A

5) [Physical training as interval or continuous training in chronic heart failure for improving functional capacity, hemodynamics and quality of life--a controlled study].

**R M Nechwatal** · C Duck · G Gruber

Zeitschrift für Kardiologie 04/2002; 91(4):328-37. • 0.97 Impact Factor

**ABSTRACT:** We conducted a three-week randomized trial comparing the improvement of functional capacity by exercise training in chronic heart failure by the steady-state (EF 27.3%, n = 20) and the interval modus (EF 29.3%, n = 20) with a control group (EF = 26.6%, n = 10). Minimal EF was 10%, the lowest maximal oxygen consumption was 9.3 ml/kg/min and the lowest cardiac output was 1.9 l/min; 9 patients had been evaluated for HTX. VO<sub>2</sub> at the anaerobic threshold and at maximal exercise increased in the continuous exercise group by 1.4 or 1.6 ml/kg/min, respectively, corresponding to an increase of 13.7% (p < 0.05) and 9.3% (p < 0.05). In the interval training group the increase was 1.3 and 1.5 ml/kg/min corresponding to 14% (p < 0.05) and 8.1% (p < 0.05). Continuous short-term exercise had no impact to central hemodynamics as pulmonary artery pressure (PA), capillary wedge pressure (pc), cardiac index (CI) or stroke volume index (SVI), whereas after interval training a significant increase at maximal exercise could be seen in CI (p < 0.05) and SVI (p < 0.01) with a concomitant drop in systemic peripheral resistance (p < 0.05) compared to the steady-state modus. Interval training was further characterized by a higher short-term but lower mean work load with a significantly smaller increase in lactate. Quality of life was improved according to the SF-36 questionnaire in both training groups but the psychologic sum factor was three times as high, increasing to 24.2% in the steady-state exercise group. It can be concluded that clinically stable patients with heart failure and even those already having been evaluated for cardiac transplantation profit from short-term physical training. Both training modalities seem equally suited to improve functional capacity. However interval training leads to more pronounced improvement in hemodynamics compared to the steady-state exercise, whereas the later had a greater impact on psychological well-being and quality of life. Patients with heart failure and severe peripheral deconditioning tolerate higher workloads with more peripheral stress by an interval training modus. Long-term training modalities need to be established to further improve and stabilize functional status.

6) Nosocomial outbreak of legionellosis in a rehabilitation center. Demonstration of potable water as a source

**R Nechwatal** · W Ehret · O J Klatte · H J Zeissler · A Prull · H Lutz

Infection 07/1993; 21(4):235-40. DOI:10.1007/BF01728897 • 2.62 Impact Factor

**ABSTRACT:** Ten patients from a rehabilitation center were admitted to hospital with serious respiratory infections within ten weeks. An outbreak of Legionnaire's disease was suspected based on the epidemic and atypical manifestation of pneumonia and could be proven microbiologically. Pulmonary and extrapulmonary complications included respiratory failure, lung abscess, transitory renal impairment in five patients and acute renal failure requiring dialysis in one, tetraparesis caused by peripheral neuropathy and acute psychosis. Three patients died despite immediate institution of therapy with erythromycin. Legionella pneumophila serogroup 1 subtype Pontiac was isolated from a bronchial lavage sample of one patient and from the water supply of the rehabilitation center. Monoclonal antibody subtyping and restriction endonuclease analysis were performed on both environmental and patient isolates. Potable water was identified as the source of the outbreak based on identical patterns on restriction endonuclease analysis. Despite thermic and chemical disinfection with chlorination (up to 15 ppm) in the rehabilitation clinic, an eleventh case of Legionnaire's disease was detected 11 months later.

7) Case study of a Legionella epidemic in a rehabilitation clinic].  
M Kramer · G Beer · **R Nechwatal** · M Exner · O J Klätte · W Ehret  
Zentralblatt für Hygiene und Umweltmedizin = International journal of hygiene and  
environmental medicine 11/1992; 193(3):262-71

**ABSTRACT:** A series of nosocomial Legionella infections in a rehabilitation center is reported. In a three months period a total of 10 pneumonias with 3 deaths occurred (8 patients, 1 companion, 1 staff member). Serologic analysis proved additional Legionella infections within the nursing staff. The warm-water system was proved to be the source of infection by isolating Legionella pneumophila serogroup 1 subtype Pontiac both in warm-water and patients samples. The air conditioning system could not be ruled out as another (secondary) route of exposure because of shortcomings in construction. Conclusions about prevention and the course of the disease are discussed and standards for warm-water and air conditioning systems are proposed.

8) Therapie des Heparin-induzierten Thrombose-Thrombozytopenie-Syndroms mit Immunglobulinen  
A. Prull · **R. Nechwatal** · H. Riedel · W. Mäurer  
DMW - Deutsche Medizinische Wochenschrift 01/1992; 117(48):1838-1842. DOI:10.1055/s-2008-1062518 · 0.54 Impact Factor

9) Fulminante venöse und arterielle Thrombosen unter Heparintherapie  
A. Prull · R. Nechwatal · W. Mäurer  
DMW - Deutsche Medizinische Wochenschrift 01/1990; 115(12):456-459. DOI:10.1055/s-2008-1065030 · 0.54 Impact Factor

## **Beteiligung an Multicenter-Studien**

### **I PIN -Studie**

1. Völler, H., et al., Long term course of cardiovascular risk factors following cardiac in-patient rehabilitation. Eur. Heart J. (Suppl.) (1999) P 3550.

2. Völler, H. et al., Lanzeitverlauf kardiovaskulärer Risikofaktoren nach stationärer Rehabilitation bei KHK-Patienten. Ztg. Kardiol. 88 (1999) Suppl., 1:1215.

3. Völler H et al. Auswirkung stationärer Rehabilitation auf kardiovaskuläre Risikofaktoren. Deutsche Medizinische Wochenschrift (2000) 124: 817- 823

## II. SOPAT-Trial

3) Suppression of paroxysmal atrial tachyarrhythmias — results of the SOPAT trial  
Monica Patten, Renke Maas, Peter Bauer, Berndt Lüderitz, Frank Sonntag, Mirosław Dłuzniewski, Robert Hatala, Grzegorz Opolski, Hans-Walter Müller, Thomas Meinertz  
European Heart Journal.2004.06.014 1395-1404 First published online: 2 August 2004

### Abstract

**Aim** The indication to treat paroxysmal atrial fibrillation (PAF) is controversial. The Suppression of Paroxysmal Atrial Tachyarrhythmias (SOPAT) trial was designed to answer the following questions: (1) What is the average rate of spontaneous events of symptomatic PAF with and without anti-arrhythmic medication? (2) what is the prevalence of severe side-effects? and (3) is the fixed combination of Quinidine+Verapamil inferior to the efficacy of sotalol or not?

**Methods and results** Within 60 months 172 centres in Germany, Poland, and The Slovak Republic prospectively enrolled 1033 patients (mean age 60 years, 62% male) with documented frequent episodes of symptomatic PAF. Patients were randomised to either Quinidine+Verapamil 480/240 mg/d (high dose; 263 patients), Quinidine+Verapamil 320/160 mg/d (low dose; 255 patients), Sotalol 320 mg/d (264 patients) or placebo (251 patients), of which 1012 patients entered the intention-to-treat analysis. The primary endpoint was the time to first recurrence of symptomatic PAF or premature discontinuation. Secondary outcome parameters were the total number of symptomatic episodes and tolerability of the tested drugs. Patients were followed for a period of up to 12 months by daily and symptom-triggered trans-telephonic ECG-monitoring (Tele-ECG).

The mean time under treatment was  $233 \hat{\pm} 152$  days. Regarding the primary endpoint, all active treatments were superior to placebo and not different from each other. A total of 756 patients reached the primary endpoint within  $105.7 \hat{\pm} 8.7$  d (mean  $\hat{\pm}$  SEM) in the placebo group, vs. Quinidine+Verapamil (high dose) ( $150.4 \hat{\pm} 10$  d,  $p=0.0061$ ), vs. Quinidine+Verapamil (low dose) ( $148.9 \hat{\pm} 10.6$  d,  $p=0.0006$ ), vs. Sotalol ( $145.6 \hat{\pm} 93$  d,  $p=0.0007$ ). All three treatments were also effective in the reduction of AF burden (days with symptomatic AF [%] mean  $\hat{\pm}$  SD, p vs. placebo): Quinidine+Verapamil (high dose) ( $3.4 \hat{\pm} 12$ ,  $p=0.0001$ ), Quinidine+Verapamil (low dose) ( $4.5 \hat{\pm} 12.3$ ,  $p=0.008$ ) and Sotalol ( $2.9 \hat{\pm} 6.5$ ,  $p=0.026$ ) compared to placebo ( $6.1 \hat{\pm} 13.5$ ). A total of four deaths, 13 syncopes, and one ventricular tachycardia (VT) occurred during the active study period, of which one death and one VT were related to Quinidine/Verapamil.

**Conclusion** Taken together, anti-arrhythmic therapy with the fixed combination of Quinidine+Verapamil is as effective as Sotalol in the reduction of the recurrence rate of symptomatic PAF with a low but definite risk of severe side-effects.