BARMELWEID

Pulmonale Rehabilitation bei PAH

9. Pulmonale-Hypertonie-Biennale 2022

St. Gallen, 23.06.2022

Dr. Marco Laures

BARMELWEID

- **Körperliche Belastung und PAH**
- **PAH- Ein rehabilitationsmedizinischer Approach**
- **Pulmonale Rehabilitation bei PAH an der Klinik Barmelweid**

Körperliche Belastung und PAH

Symptome und Risiko

WHO Class I	WHO Class II	WHO Class III	WHO Class IV
Class I – Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnoea or fatigue, chest pain, or near syncope.	Class II – Patients with pulmonary hypertension resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnoea or fatigue, chest pain, or near syncope.	Class III – Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnoea or fatigue, chest pain, or near syncope.	Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnoea and/or fatigue may be present even at rest. Discomfort is increased by any physical activity.

Adapted from: Barst RJ, McGoon M, Torbicki A *et al. J Am Coll Cardiol* 2004;43:40S–47S.

TABLE 1. Risk Assessment in PAH[1]

Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5%-10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope[b]	Repeated syncope[c]
WHO functional class	I, II	III	IV
6MWD	>440 m	165-440 m	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15 mL/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11-15 mL/min/kg (35%-65% pred.) VE/VCO_2 slope 36-44.9	Peak VO_2 <11 mL/min/kg (<35% pred.) VE/VCO_2 slope ≥45
NT-proBNP plasma levels	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50-300 ng/L NT-proBNP 300-1400 ng/L	BNP >300 ng/L NT-proBNP >1400 ng/L
Imaging (echocardiography, CMR imaging)	RA area <18 cm^2 No pericardial effusion	RA area 18-26 cm^2 No or minimal pericardial effusion	RA area >26 cm^2 Pericardial effusion
Hemodynamics	RAP <8 mm Hg CI ≥2.5 L/min/m^2 SvO_2 >65%	RAP 8-14 mm Hg CI 2.0-2.4 L/min/m^2 SvO_2 60%-65%	RAP >14 mm Hg CI <2.0 L/min/m^2 SvO_2 <60%

Körperliche Belastung und PAH

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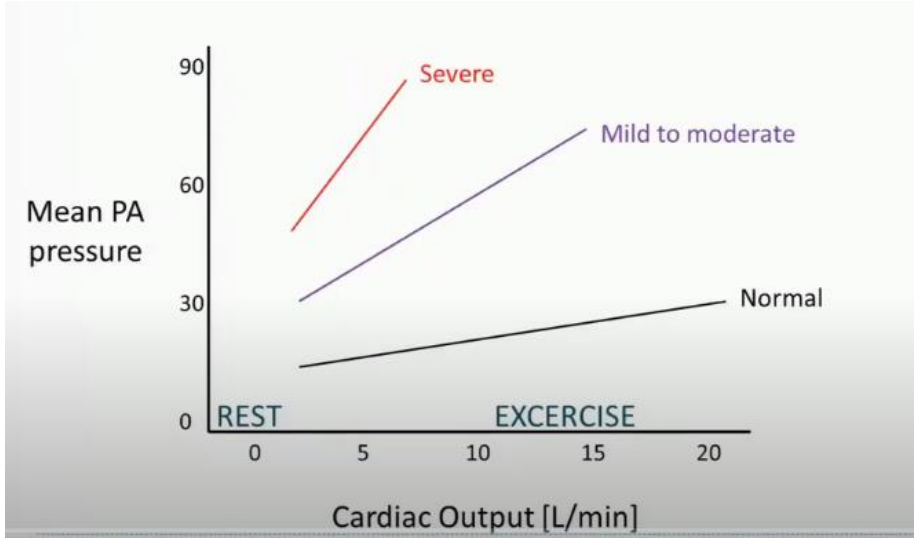
- Belastungsdyspnoe, (Prä-)Synkopen
- muskuläre Dysfunktion
- Angst und Depression

- physische Inaktivität
- Reduzierte Leistungsfähigkeit
- Reduzierte QoL

Osadnik CR, Rodrigues FMM, Camillo CA, Loeckx M, Janssens W, Dooms C, et al. Principles of Rehabilitation and Reactivation. Respiration. 2015;89(1):2–11.

Körperlichen Trainings bei PAH - Con



Erhöhtes Risiko eines/r

- Plötzlichen Herztodes
- Exazerbation des Rechtsherzversagens
- Zunahme des pulmonalen Remodelings und Zunahme der PH

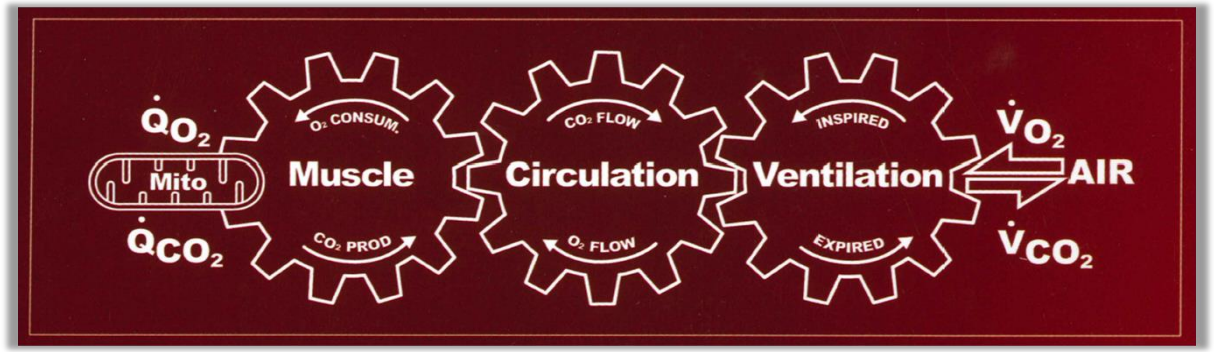
1. Gaine SP, Rubin LJ. Primary pulmonary hypertension. Lancet Lond Engl. 1998 Aug 29;352(9129):719–25.

Hauptrisiken körperlichen Trainings bei PAH

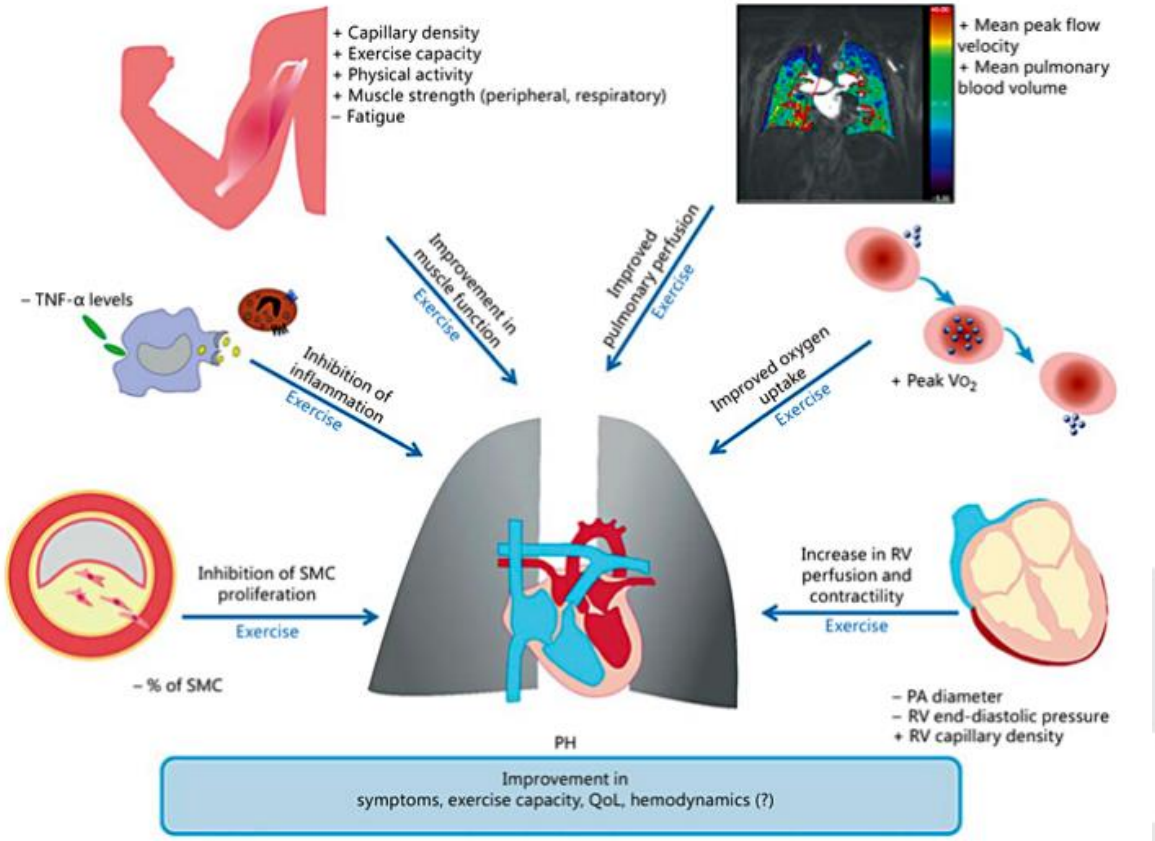
- Hämodynamische Auswirkungen einer plötzlichen Verschlechterung der RV-Funktion (CO↓)
- Arrhythmien und Synkopen

1. La Gerche A, Claessen G. Is exercise good for the right ventricle? Concepts for health and disease. Can J Cardiol. 2015 Apr;31(4):502–8..
2. Mar PL, Nwazue V, Black BK, Biaggioni I, Diedrich A, Paranjape SY, et al. Valsalva Maneuver in Pulmonary Arterial Hypertension: Susceptibility to Syncope and Autonomic Dysfunction. Chest. 2016;149(5):1252–60.

Körperlichen Trainings bei PAH - Pro



1. K. Wasserman: Principles of Exercise Testing and Interpretation. Including Pathophysiology and Clinical Applications. Fifth edition. Lippincott Williams and Wilkins Verlag, Philadelphia, 2011.



Marra AM, Egenlauf B, Bossone E, Eichstaedt C, Grünig E, Ehlken N. Principles of rehabilitation and reactivation: pulmonary hypertension. Respiration. 2015;89(4):265–73.

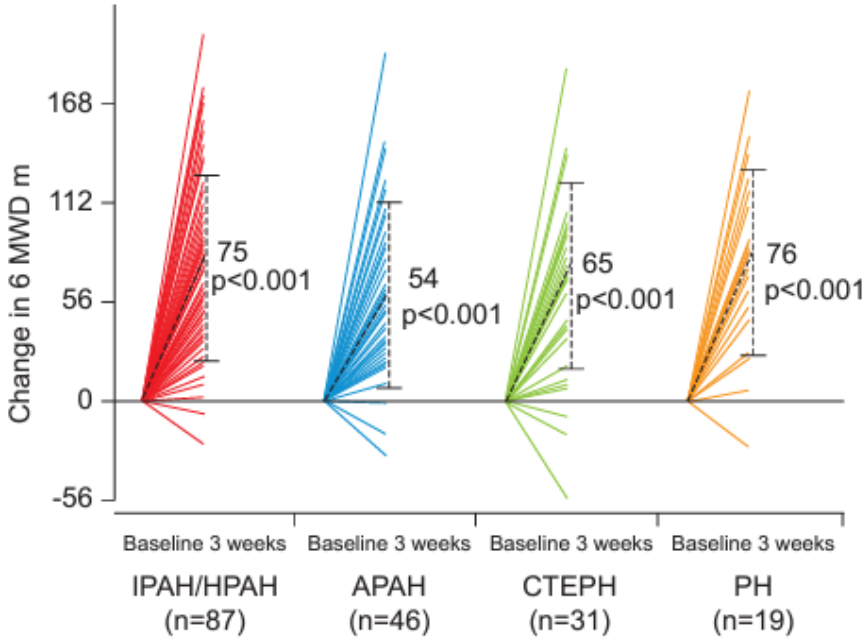
Safety and efficacy of exercise training in various forms of pulmonary hypertension

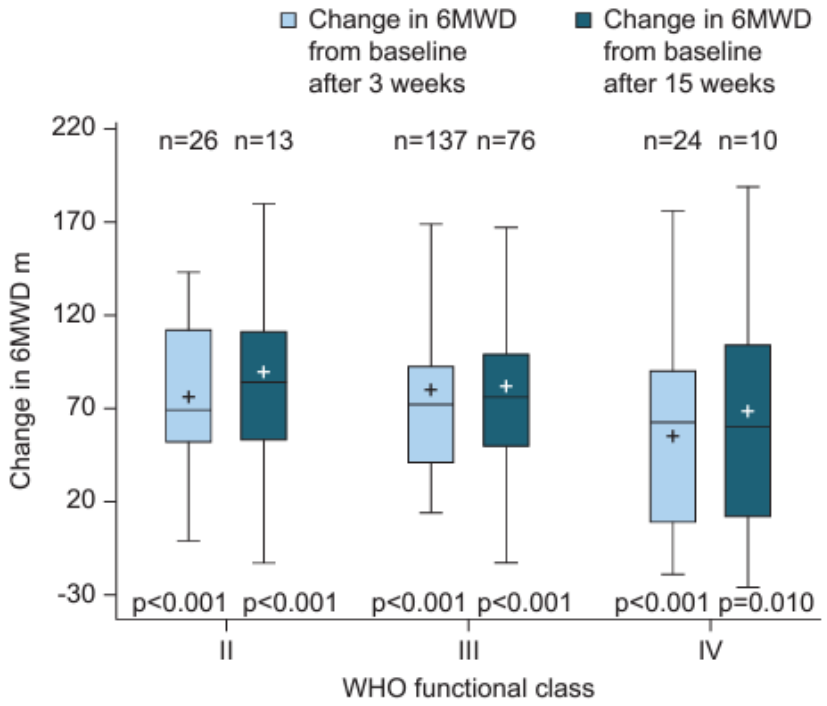
Ekkehard Grünig*,+++, Mona Lichtblau*,+++, Nicola Ehlken*, Hossein A. Ghofrani#, Frank Reichenberger#, Gerd Staehler¶, Michael Halank+, Christine Fischer§, Hans-Jürgen Seyfarth∫, Hans Klose**, Andreas Meyer##, Stephan Sorichter¶¶, Heinrike Wilkens++, Stephan Rosenkranz§§, Christian Opitz∫∫, Hanno Leuchte***, Gabriele Karger###, Rudolf Speich¶¶¶ and Christian Nagel*

PH (n= 183)

3w inhospital
+12w home-training
(u.a. Velo10-60W, Hf 60-80%Hfmax)

6MWD





Adverse events 13%,(respiratory infections, syncope or presyncope)

Grünig E, Lichtblau M et al. Eur Resp. J 2012

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PH (n= 183)

3w inhospital
+12w home-training
(u.a. Velo 10-60W, Hf 60-80%Hfmax)

VO2max
(sek .Endpunkt)

	Baseline		3 weeks				15 weeks			
	Mean ± SD	95% CI	Mean ± SD	Median	95% CI	p-value	Mean ± SD	Median	95% CI	p-value
Cardiopulmonary exercise testing										
Peak $\dot{V}O_2$ per kg mL·min^{-1}·kg^{-1}	12.2 ± 3.5		13.6 ± 4			<0.001	13.9 ± 3.8			<0.001
Peak $\dot{V}O_2$ mL·min^{-1}	907 ± 276		1006 ± 308			<0.001	1011 ± 292			<0.001

Grünig E, Lichtblau M et al. Eur Resp. J 2012

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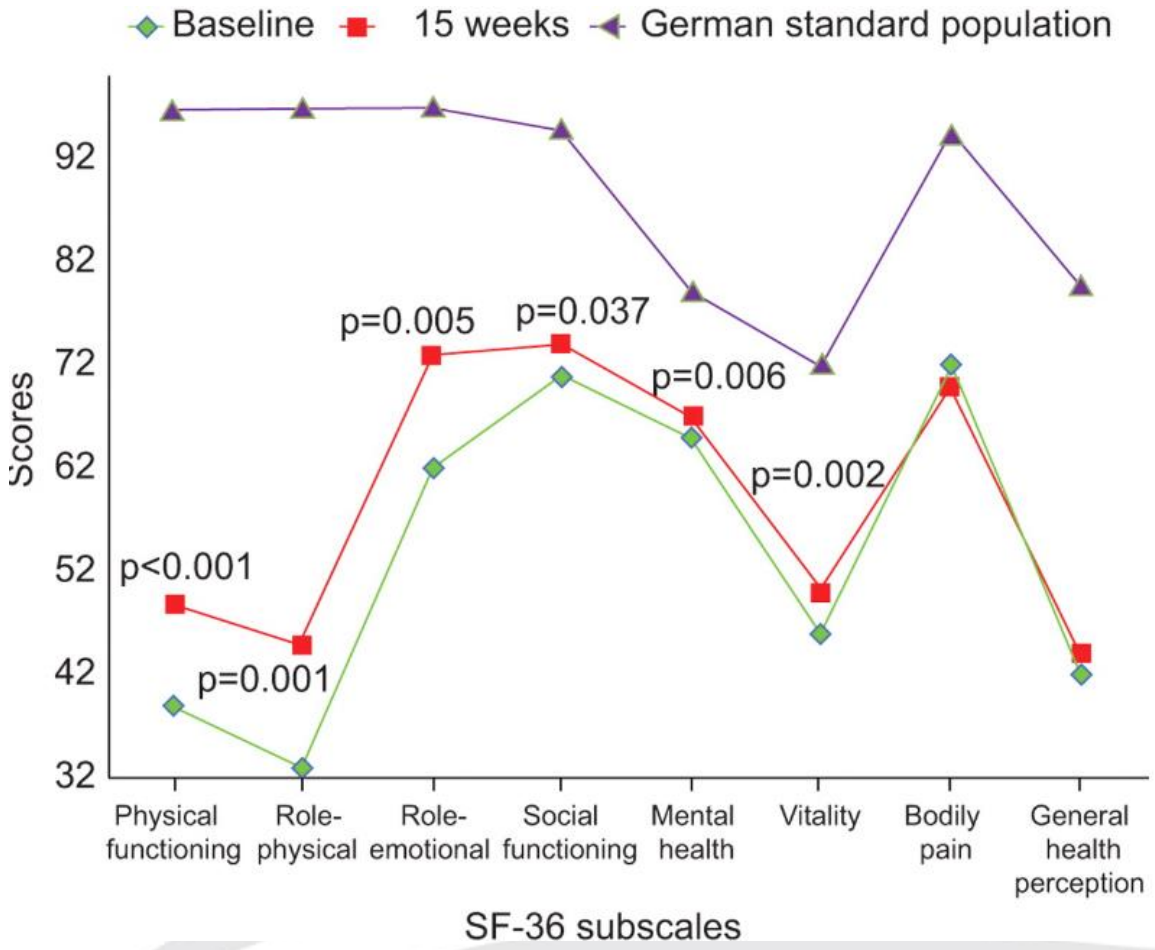
PH (n= 183)

3w inhospital
+12w home-training
(u.a. Velo10-60W, Hf 60-80%Hfmax)

QoL, SF-36
(sek .Endpunkt)



Grünig E, Lichtblau M et al. Eur Resp. J 2012

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

European Heart Journal (2016) **37**, 35–44
doi:10.1093/eurheartj/ehv337

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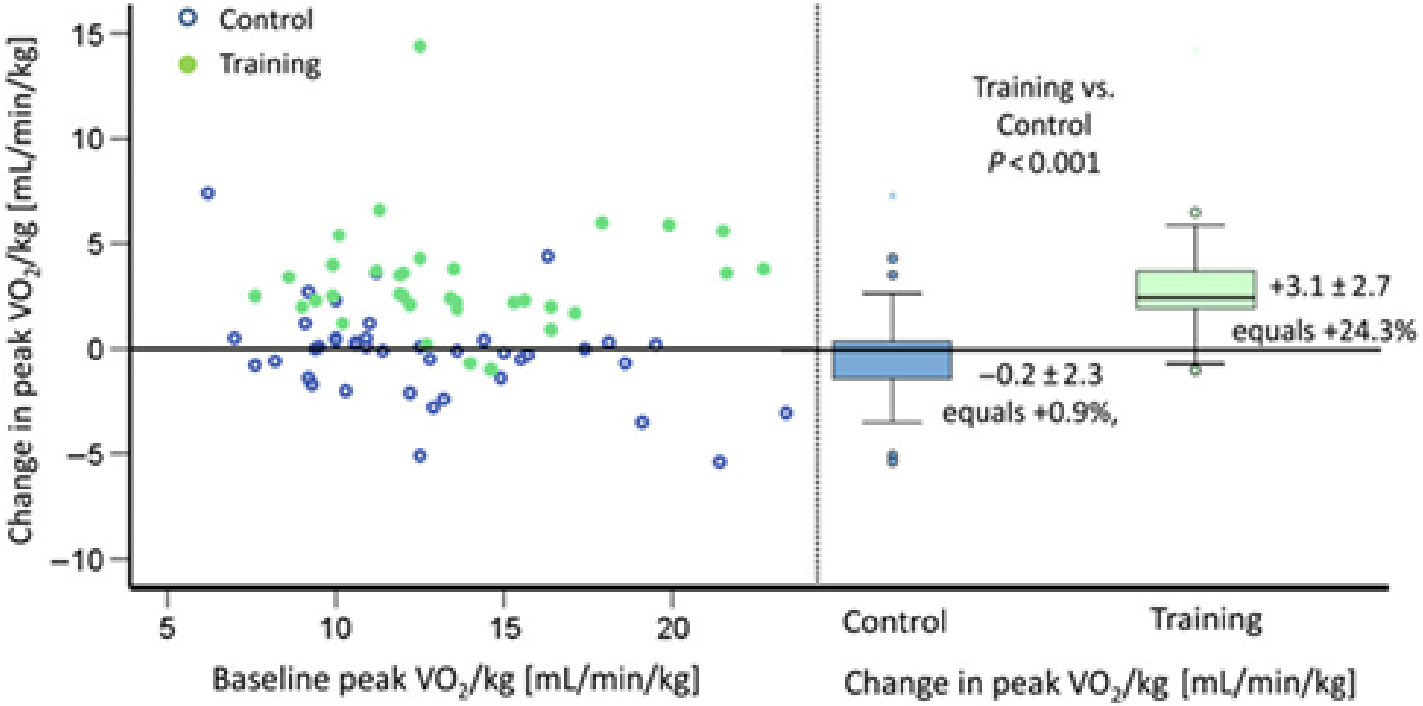
IPAH + inoperable CTEPH
(n= 79)

15w (3/12) training (n=38)
vs.
usual care (n=41)

VO2max



Ehlken Nicola, Lichtblau M et al. Europ. Heart J 2016

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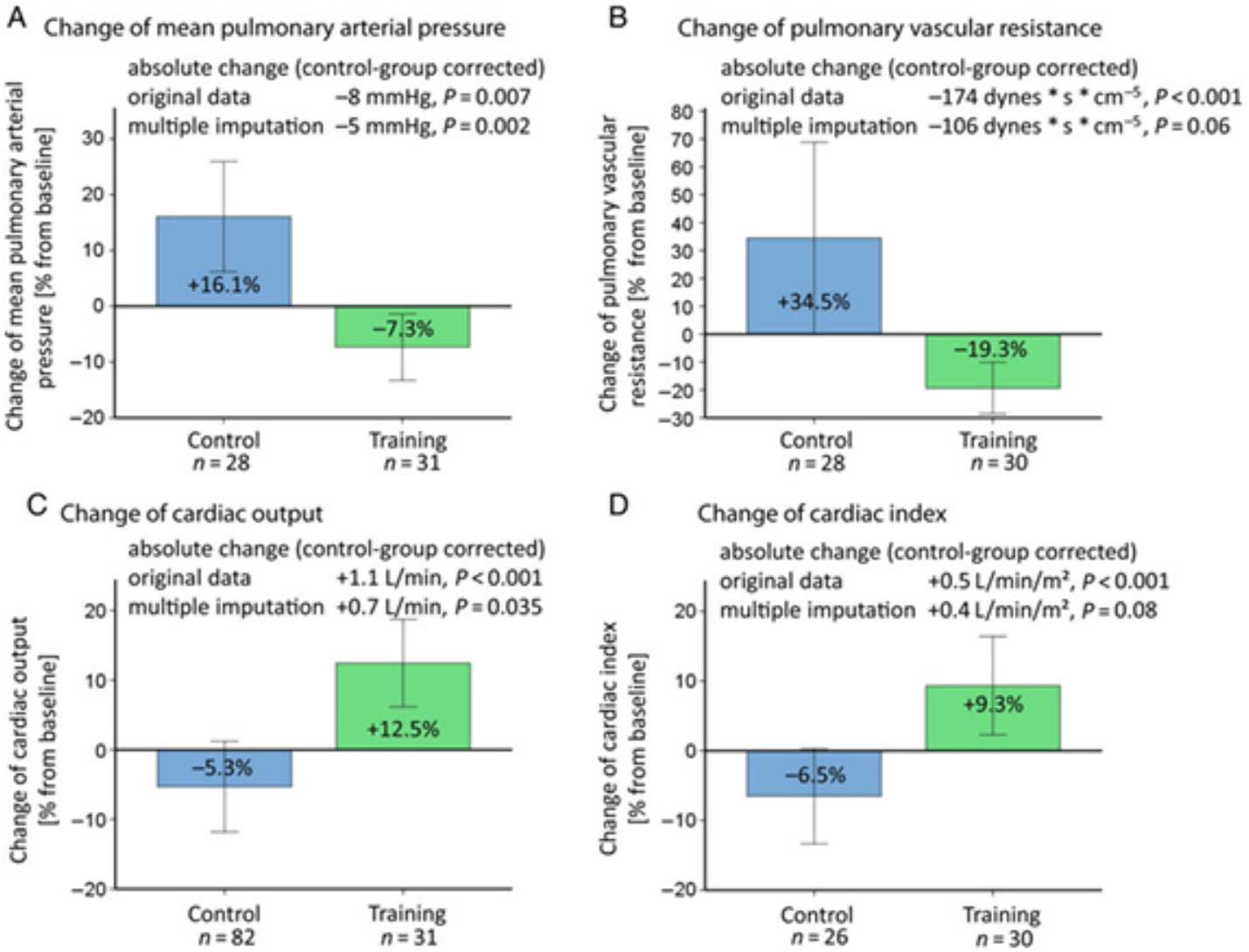
IPAH + inoperable CTEPH
(n= 74)

15w (3/12) training (n=34)
vs.
usual care (n=40)

Rechtsherzkatheter
(sek. Endpunkt)



Ehlken Nicola, Lichtblau M et al. Europ. Heart J 2016

ESC 2021

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 2284–2295
doi:10.1093/eurheartj/ehaa696

CLINICAL RESEARCH
Thrombosis and antithrombotic treatment

Standardized exercise training is feasible, safe, and effective in pulmonary arterial and chronic thromboembolic pulmonary hypertension: results from a large European multicentre randomized controlled trial

Ekkehard Grünig[1]*†, Alison MacKenzie [2†], Andrew J. Peacock [2], Christina A. Eichstaedt[1,3], Nicola Benjamin[1], Robert Nechwatal [4], Silvia Ulrich [5], Stéphanie Saxer [5], Maurizio Bussotti [6], Marinella Sommaruga [6], Stefano Ghio [7], Lina Gumbiene [8,9], Eglė Palevičiūtė[8,9], Elena Jurevičienė[8,9], Antonio Cittadini[10], Anna A. Stanziola[11], Alberto M. Marra [1,12], Gabor Kovacs [13,14], Horst Olschewski [13,14], Joan-Albert Barberà[15], Isabel Blanco[15], Martijn A. Spruit [16,17,18,19], Frits M.E. Franssen [20], Anton Vonk Noordegraaf[21], Abílio Reis [22], Mário Santos [22], Sofia Gonçalves Viamonte[23], Heleen Demeyer [24,25,26], Marion Delcroix [24], Eduardo Bossone [27‡], and Martin Johnson [2‡]

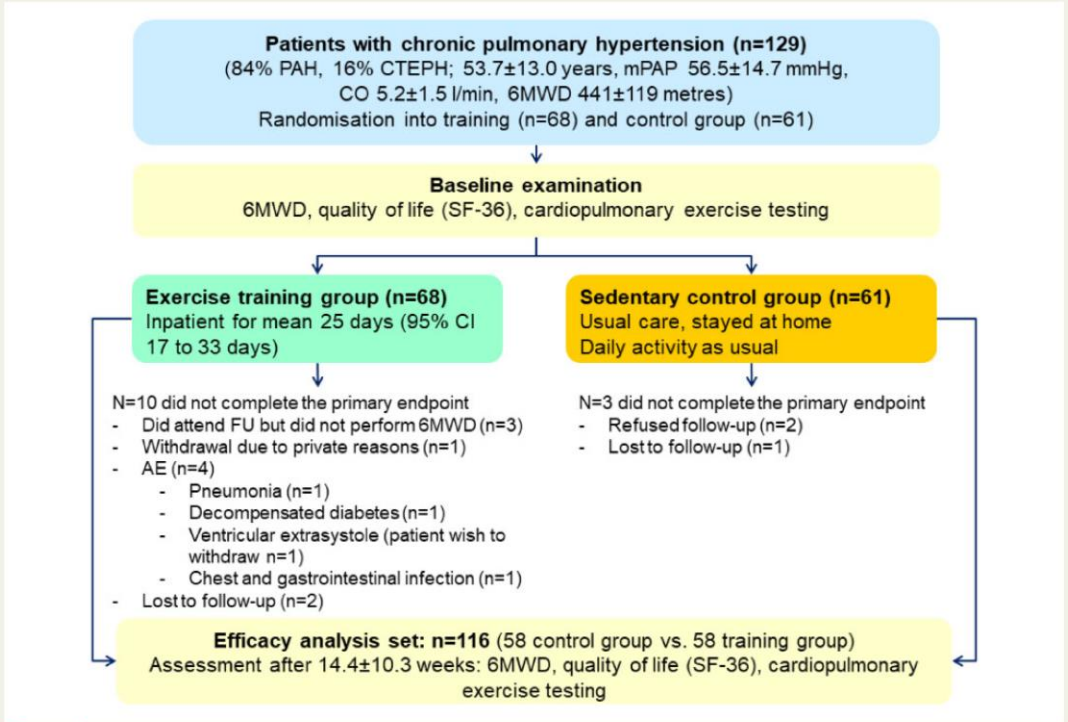


Figure 1 Study flow-chart. This flow-chart gives the course of the study, patient randomization, assessments, and definition of dropouts. 6MWD, 6-min walking distance; AE, adverse event; CI, confidence interval; CO, cardiac output; CTEPH, chronic thromboembolic pulmonary hypertension; FU, follow-up; mPAP, mean pulmonary artery pressure; PAH, pulmonary arterial hypertension.

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Characteristic	Control group (*n*=58)				Training group (*n*=58)			
WHO-FC class number (%)								
I	0				1		(1.7%)	
II	34		(58.6%)		26		(44.8%)	
III	24		(41.4%)		30		(51.7%)	
IV	0				1		(1.7%)	
6-min walking test								
6MWD (m)	447.4	±	120.2	(415.8 to 479.0)	447.2	±	117.7	(416.2 478.1)

Grünig E *et al.* European Heart Journal 2021

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Characteristic	Control group (n=58)					Training group (n=58)				
Cardiopulmonary exercise testing (CPET) with stress echocardiography										
Peak heart rate (/min)	123.0	±	23.3	(115.8 to 130.1)	43	134.1	±	22.9	(127.2 141.1)	
Peak SaO_2 (%)	90.0	±	7.2	(87.7 to 92.2)	41	90.5	±	7.1	(88.3 t 92.7)	
Peak VO_2 (mL/min/kg)	15.3	±	4.3	(14.2 to 16.5)	53	14.2	±	5.2	(12.8 t 15.6)	
Peak VO_2 % predicted (%)	68.5	±	20.8	(61.9 to 75.0)	41	68.7	±	51.5	(52.9 t 84.6)	
Peak workload (W)	81.6	±	30.2	(71.9 to 91.2)	40	81.2	±	27.1	(79.3 t 89.4)	

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ESC European Society of Cardiology
European Heart Journal (2021) 42, 2284–2295
doi:10.1093/eurheartj/ehab096

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BARMELWEID

PAH 84%/CTEPH 16%

Excercise training (n=58)
Usual care (n=58)

6 MWD post vs. pre

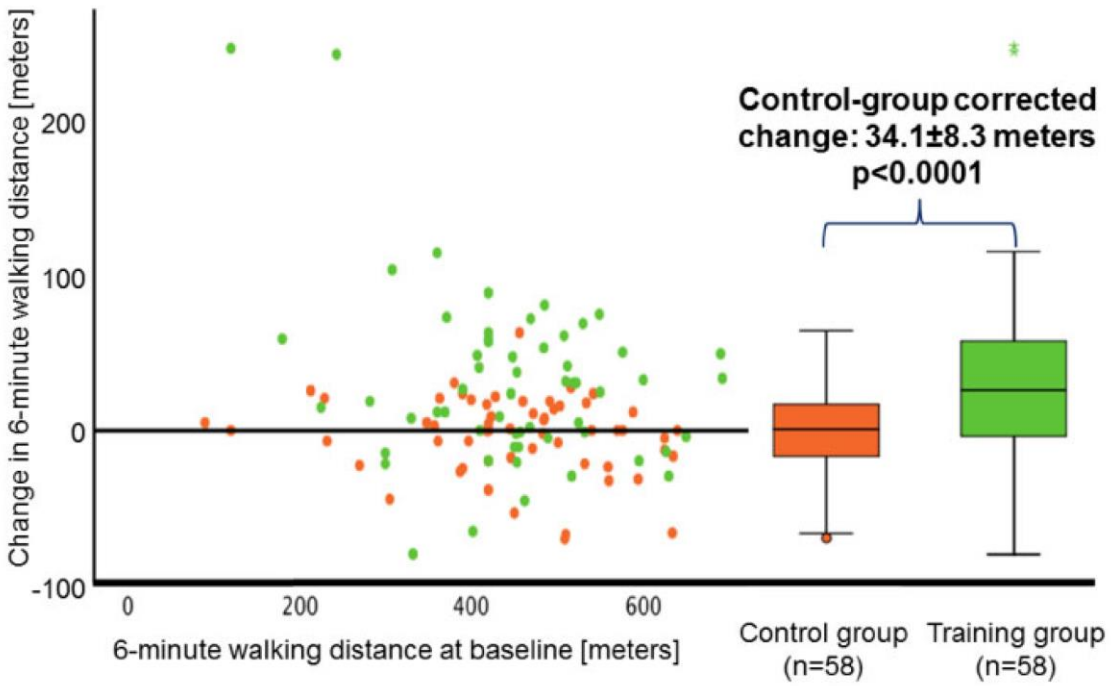

Figure 2 Primary endpoint 6-min walking distance. Patients of the training group significantly improved in 6MWD compared with the control group by 34.1±8.3 m ($P < 0.0001$).

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PAH 84%/CTEPH 16%

Excercise training (n=58)
Sedentary (n=58)

QoL
(sek. Endpunkt)

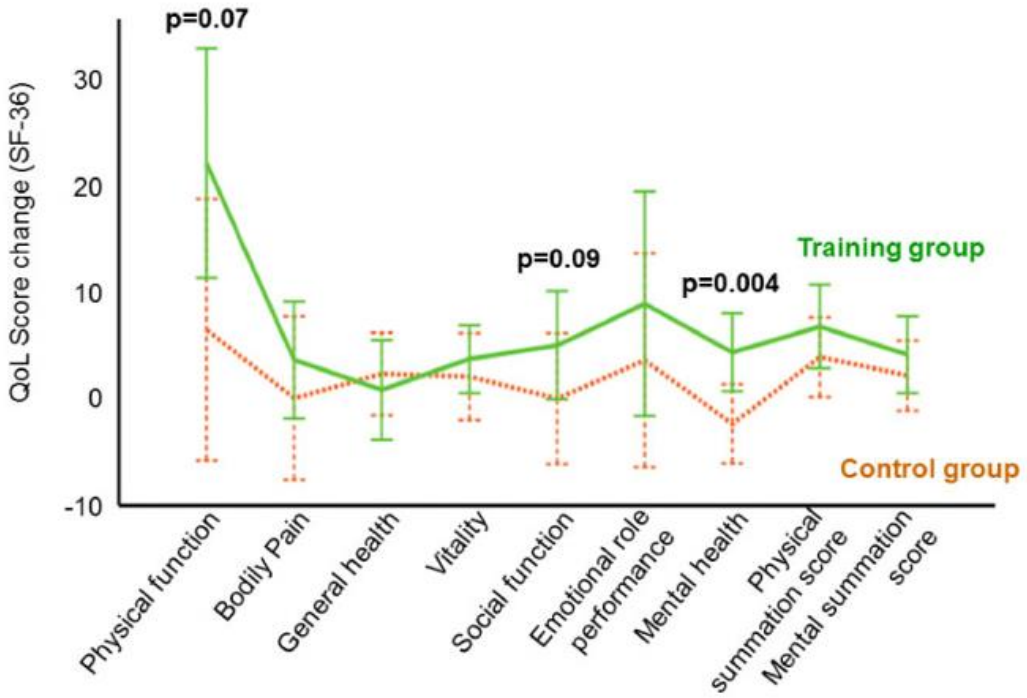

Figure 3 Secondary endpoints: quality of life. The secondary endpoint quality of life (QoL) significantly improved in the subscale mental health in the training group compared with the control group ($P = 0.004$). Two further subscales were significant in trend (physical function $P = 0.07$, social function $P = 0.09$).

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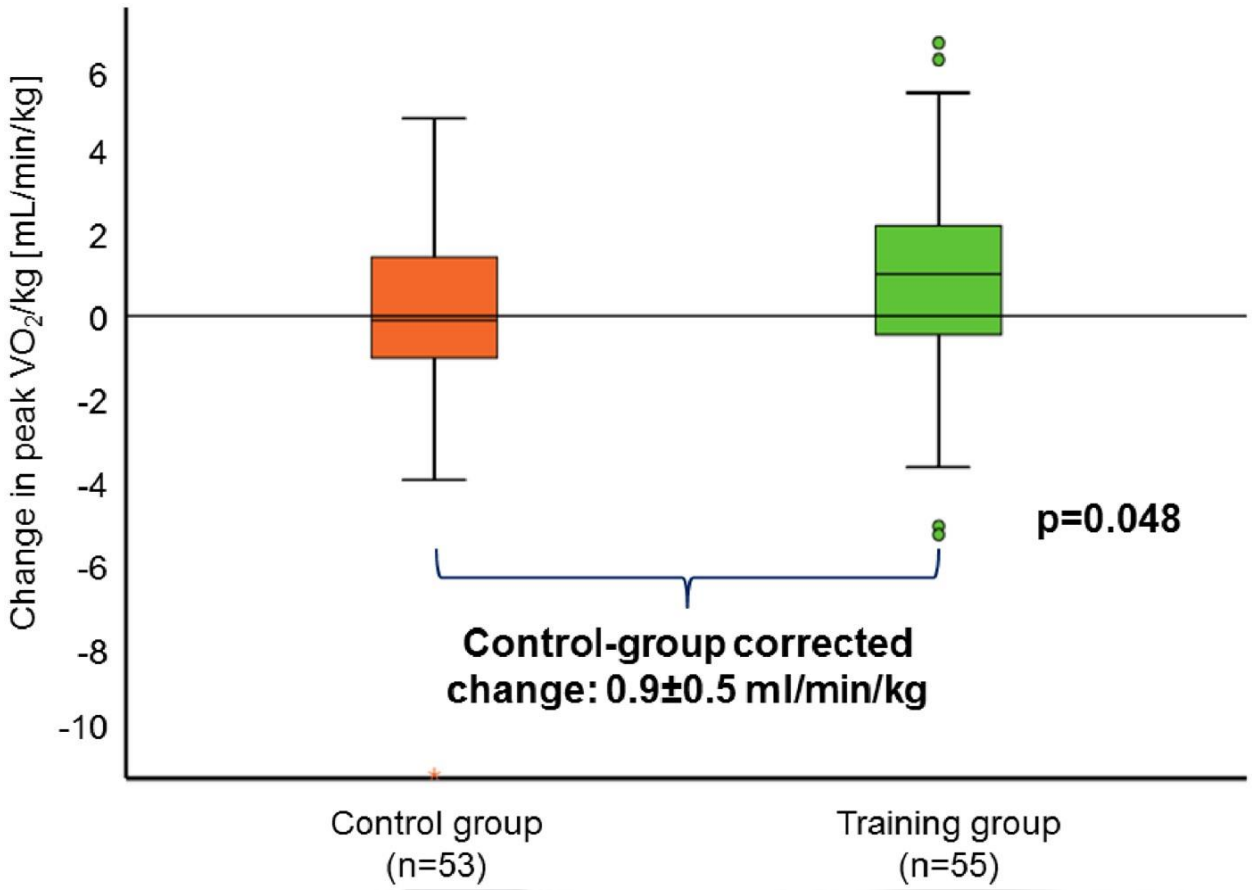
BARMELWEID

PAH 84%/CTEPH 16%

Excercise training (n=58)
Sedentary (n=58)

VO2max
(sek. Endpunkt)



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BARMELWEID

PAH 84%/CTEPH 16%

(n=116)

Excercise training (n=58)
Sedentary (n=58)

Adverse events

Table 3 Adverse events with occurrence ≥5%

Adverse events	Group: Control (*n* = 47)	Group: Training (*n* = 52)	Total
Arrhythmia of any kind	5	3	8
Respiratory infection	3	4	7
Total	8	7	15
Serious adverse events			
Diabetes, decompensated	0	1	1
Oedema, generalised	0	1	1
Haemoptysis	1	0	1
Stroke	0	1	1
Total	1	3	4

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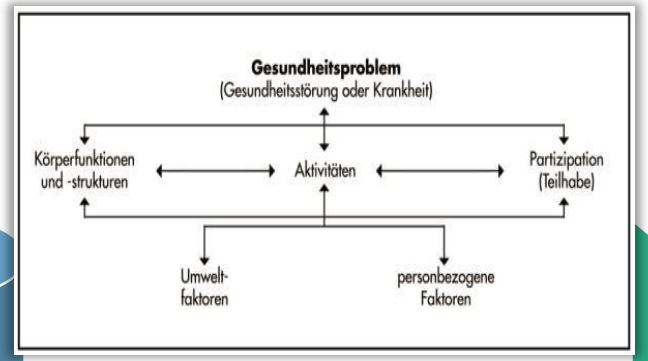
Die Sichtweise der Pulmonalen Rehabilitation

Funktionelle Einschränkungen anstelle Diagnosen



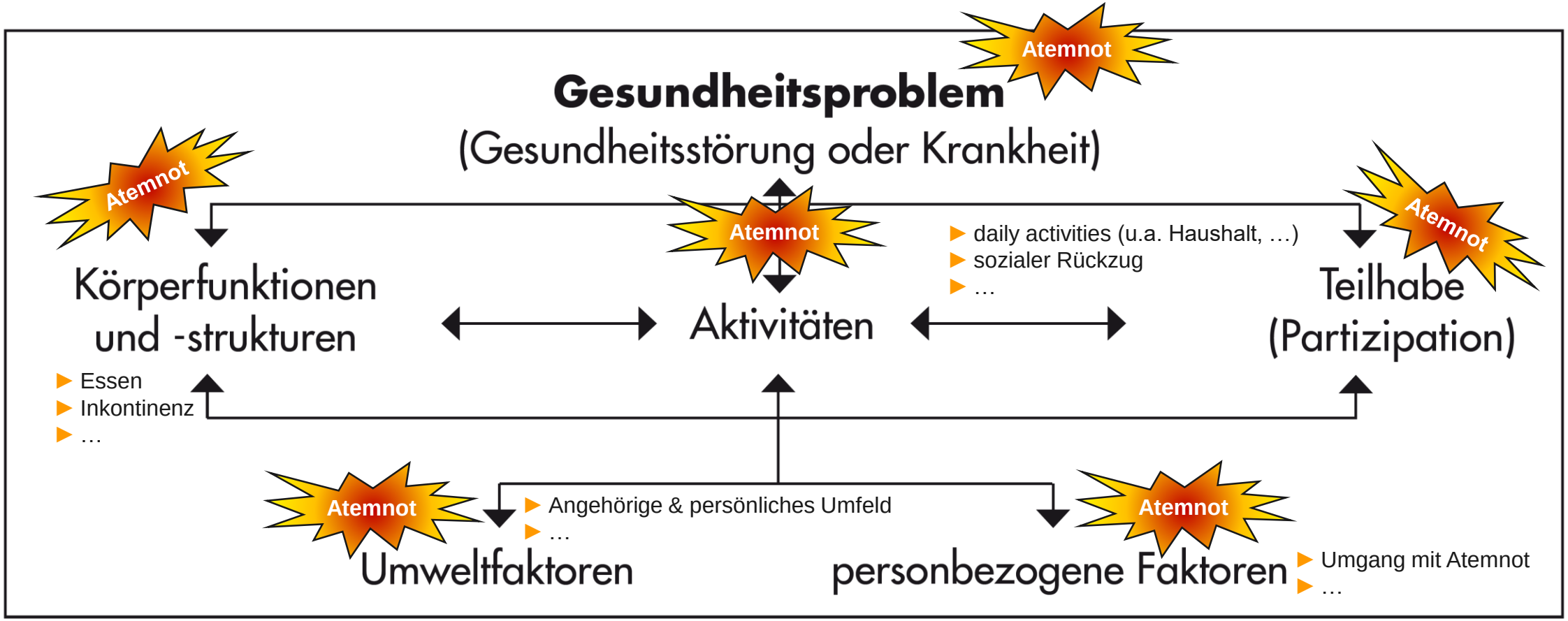
Diagnose

Funktion

International Classification of Functioning, Disability, and Health (ICF)
World Health Organization (WHO)

Symptome, Funktion und ICF

Wie wir in der Rehabilitation denken müssen



Bio-psycho-soziales Modell der Internationalen Klassifikation der Funktionsfähigkeit, Behinderung und Gesundheit der WHO (ICF)

Abbildung aus: Bundesarbeitsgemeinschaft für Rehabilitation (BAR): Rahmenempfehlungen zur ambulanten pneumologischen Rehabilitation, 2008, S. 11

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Systematic Review on Outcome Measures PR / PH

BARMELWEID

SYSTEMATIC REVIEWS

Outcome Measures Used in Studies of Rehabilitation in Pulmonary Hypertension

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	Studies [*n* (%)]			
	2006–2009 (*n* = 2)	2010–2014 (*n* = 16)	2015–2019 (*n* = 16)	Total (*n* = 34)
Study design				
Prospective single cohort	1 (50)	8 (50)	4 (25)	13 (38)
RCT	1 (50)	3 (19)	8 (50)	12 (3)
Protocol	0 (0)	1 (6)	2 (13)	3 (9)
Nonrandomized two-armed	0 (0)	3 (19)	0 (0)	3 (9)
Retrospective	0 (0)	1 (6)	1 (6)	2 (6)
Case series	0 (0)	0 (0)	1 (6)	1 (3)
Patient population				
PAH	1 (50)	8 (50)	10 (63)	19 (56)
PH	1 (50)	5 (31)	4 (25)	10 (29)
PAH or CTEPH	0 (0)	1 (6)	2 (13)	3 (9)
CTEPH	0 (0)	2 (13)	0 (0)	2 (6)
Intervention				
Whole-body exercise training	2 (100)	14 (88)	10 (63)	26 (76)
Walking program	0 (0)	2 (12.5)	1 (6)	3 (9)
Inspiratory muscle training	0 (0)	0 (0)	2 (13)	2 (6)
Oscillation plate	0 (0)	0 (0)	1 (6)	1 (3)
Yoga	0 (0)	0 (0)	1 (6)	1 (3)
Mindfulness	0 (0)	0 (0)	1 (6)	1 (3)
Intervention period				
Up to 1 mo	0 (0)	0 (0)	2 (13)	2 (6)
2–4 mo	2 (100)	15 (94)	13 (81)	30 (89)
5–12 mo	0	1 (6)	1 (6)	2 (6)

Definition of abbreviations: CTEPH = chronic thromboembolic pulmonary hypertension; PAH = pulmonary arterial hypertension; PH = pulmonary hypertension; RCT = randomized controlled trial.

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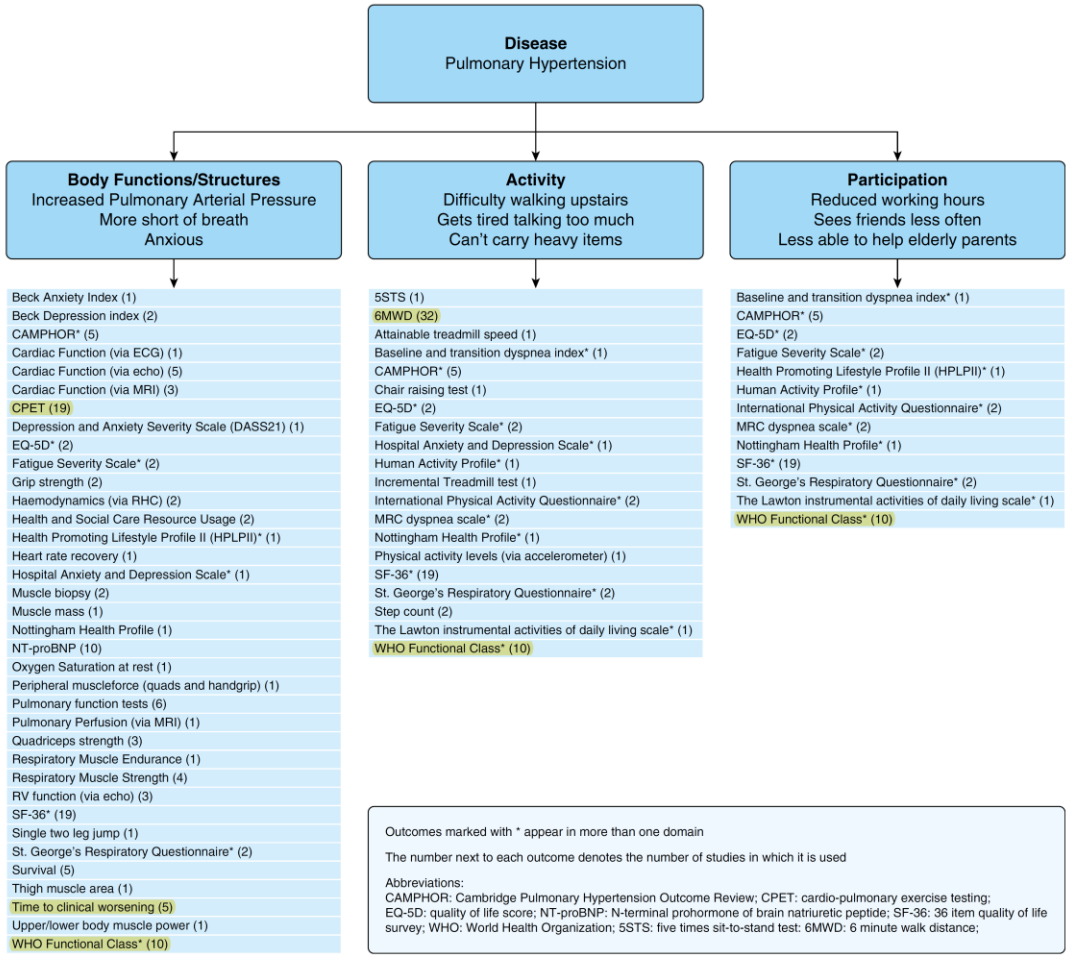


Figure 2. International Classification for Functioning, Disability and Health classification. 5STS = five times sit-to-stand test: 6MWD = 6-minute walk distance; CAMPHOR = Cambridge Pulmonary Hypertension Outcome Review; CPET = cardiopulmonary exercise testing; ECG = electrocardiogram; EQ-5D = quality of life score; MRC = Medical Research Council; MRI = magnetic resonance imaging; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; RHC = right heart catheter; RV = right ventricle; SF-36 = 36-item quality of life survey; WHO = World Health Organization.

Conclusions

Studies of rehabilitation in PH have focused primarily on measures of Body Functions/ Structure; the impact in other domains is less well characterized. Greater inclusion of outcome measures reflecting activity and participation in society is needed to allow assessment of the wider impact of rehabilitation in patients with PH. ■

BARMELWEID

USZ Universitäts Spital Zürich

Die PAH-Rehabilitation an der Klinik Barmelweid

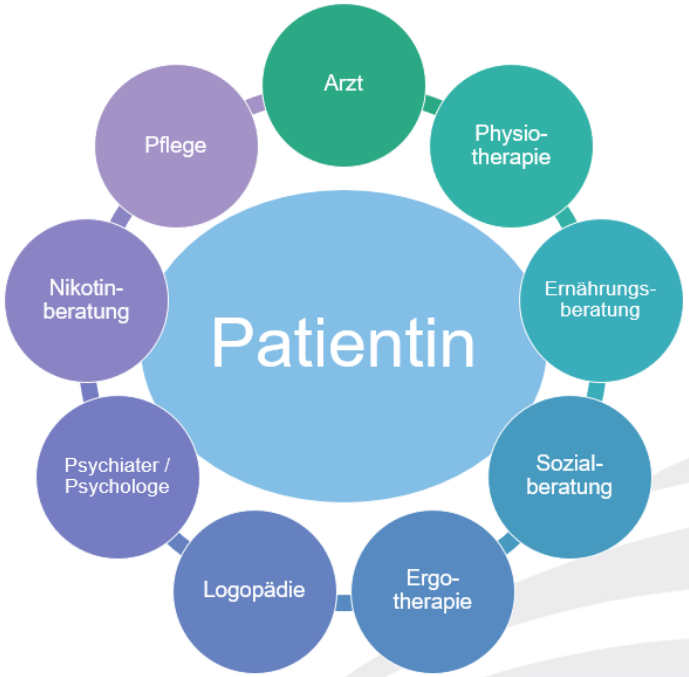
PAH-Rehabilitation Assessment

- Anamnese/Zielerfassung durch Arzt, Pflege und Physiotherapie

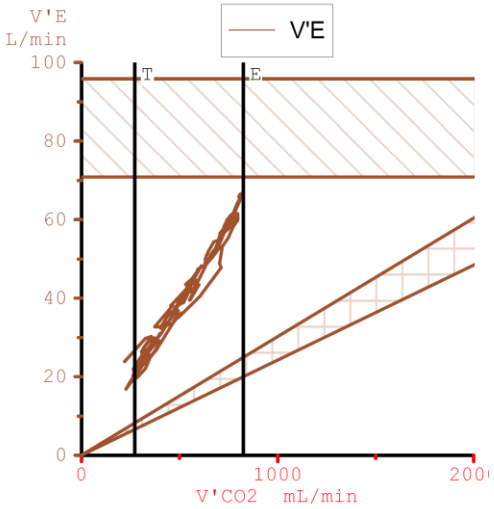
- Fragebögen: CRQ, FIM, HAD-S, mMRC

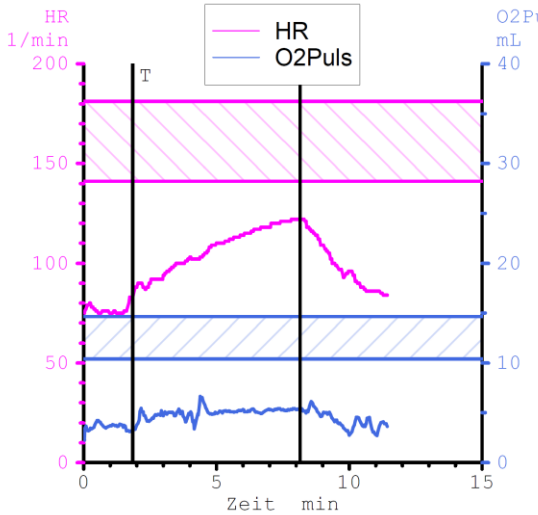
- Lungenfunktion, 6-Minuten-Gehtest, Spiroergometrie

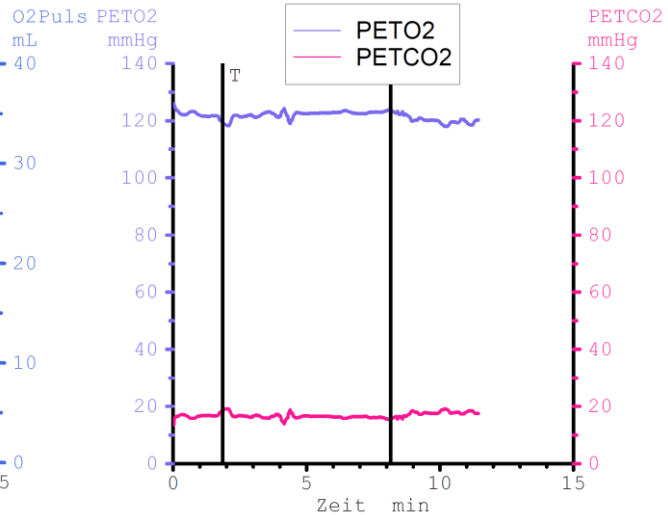
→ Interprofessionelle Festlegung der Reha-Ziele



Assessment - Spiroergometrie







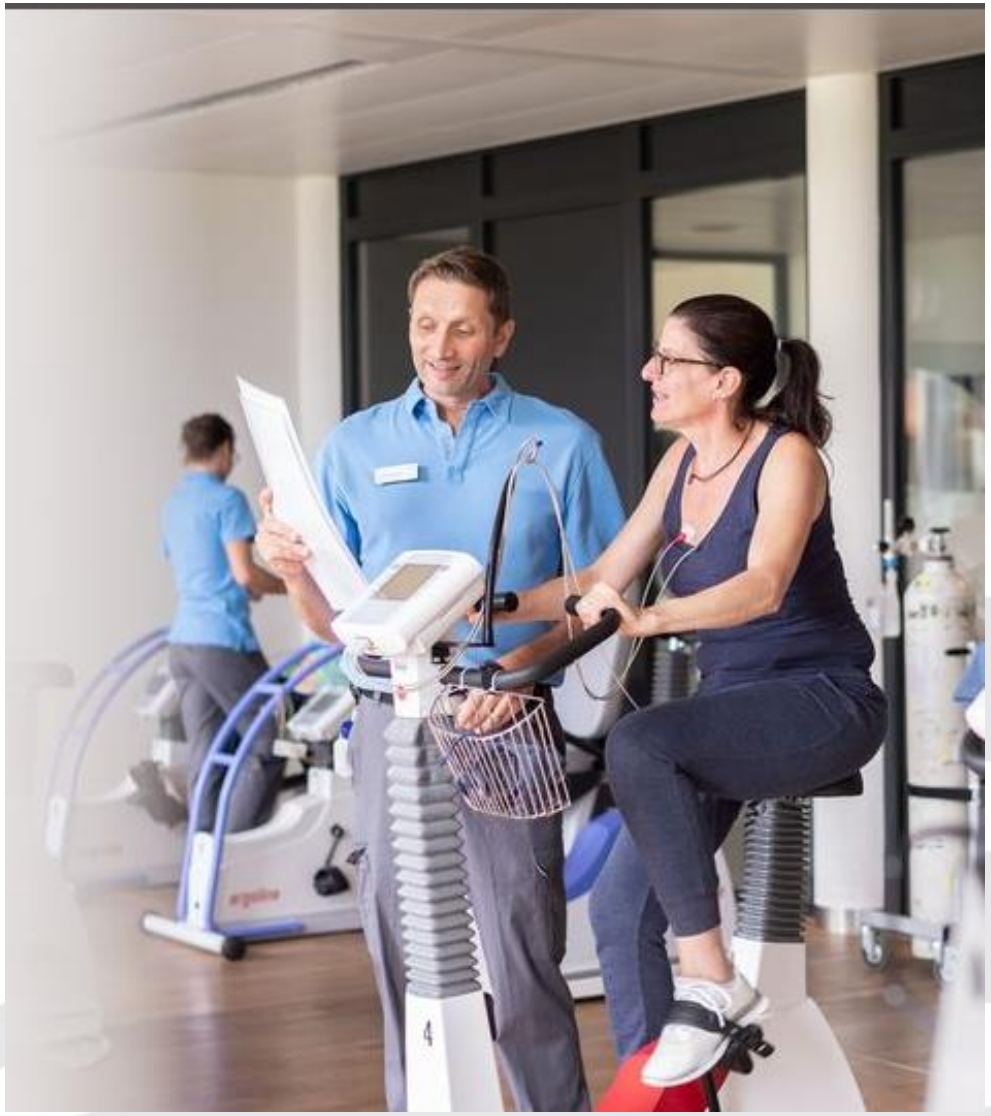
Bemerkung				-
Liter flow		L/min		nativ
Temperatur		°C		37.0
FO2		%		21.0
pH(T) (Art.)	7.350 - 7.450			7.47 ↑
pCO2(T) (Art.)	35 - 48	mmHg		30.5 ↓
pO2(T) (Art.)	83 - 108	mmHg		65.4 ↓
pO2 (A-a) (Art.)		mmHg		36.6 ↑
O2-Sättigung (Art.)		%		93.2
Bicarbonat (Art.)	21.8 - 26.2	mmol/l		22.0 ↓
cBase(Ecf) (Art.)	-3.0 - 2.0	mmol/l		-1.2
CtO2 (Art.)	18.8 - 22.3	Vol%		17.9 ↓
p50c (Art.)	24 - 28	mmHg		25
Hämoglobin (Art.) (POC)	120 - 160	g/l		140
FO2Hb (Art.)	94 - 98	%		91 ↓
FCOHb (Art.)	< 1.5	%		1.4
FMetHb (Art.)	< 1.5	%		0.7
Hämatokrit (POC)	38 - 51	%		43

Therapien der PAH Rehabilitation Barmelweid (Σ >540 minutes per week)

- Ausdauer (Fahrrad, Wandern)
- Kraft
- Gymnastik
- Mentales Training
- Entspannung
- Schulungen
- Individuelle Therapien
- PH-Gruppen wenn möglich
- Weitere Therapien je nach Situation

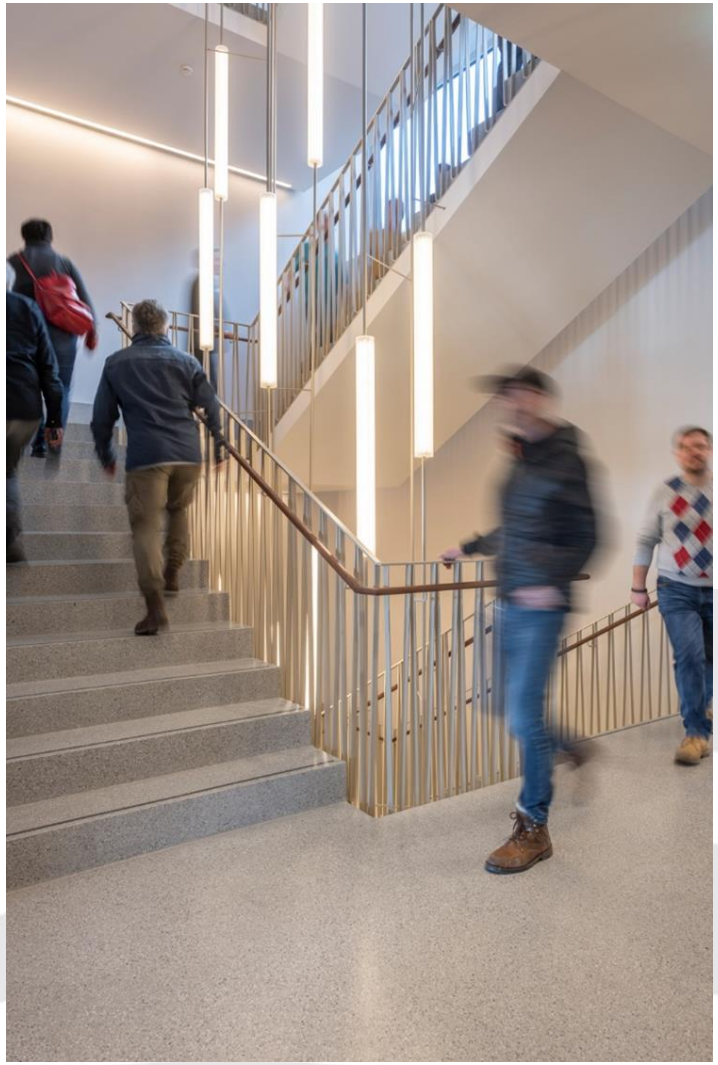
PAH-Rehabilitation – Ausdauer- und Krafttraining

- Maximum heart rate 120bpm
- VAS max 4/10
- Ergometertraining: Intervalltraining (LIIT) mit Obergrenze 50% der Wattmax max. 50/15W
- SpO2-Ziel >88%
- Vermeidung Pressatmung
- Keine schweren Gewichte (max. 1-2kg)
- Kraftübungen zu Beginn unilateral im Sitzen
- Fokus auf Wahrnehmung und Oekonomisierung der Atmung



PAH-Rehabilitation – Mentales Gehtraining

- Einzelphysiotherapie
- Entwicklung und gedankliche Visualisierung ausdauernden Gehens in der (Ebene)
- Entwicklung und gedankliche Visualisierung für Gehen in Anforderungssituation (Zeitdruck/Treppe)
- Mentales Trainieren der Vorstellungen
- Mentales und motorische Training im Wechsel



Erfahrung aus der PAH-Rehabilitation Barmelweid

BARMELWEID

Unsere Patienten sind…

- in der Regel klinisch stabil
  (bei klinisch instabiler Situation führen wir bei PH keine PR durch)
- gut kontrolliert mit ausgebauter Medikation entsprechend den aktuellen Empfehlungen
- sehr gut informiert und voller Erwartungen
- hoch motiviert
- oft enttäuscht (relative tiefe Therapieintensität, langsamer Fortschritt)
- enttäuscht da keine PH-Gruppen bestehen (wenige Patienten mit PH / seltene Krankheit)
- zeigen nur sehr selten Komplikationen

Rehabilitation bei PAH

BARMELWEID

Evidenz

- Körperliches Training bei PAH: Solide Evidenz für die Wirksamkeit (6 MWT, VO2max, (Hämodynamik) QoL) und Sicherheit

Voraussetzungen / Erfolgsfaktoren

- klinisch stabiler Zustand unter ausgebauter medikamentöser Therapie
- Zentrum/Netzwerk mit entsprechender Kompetenz

Ziele der weiteren Entwicklung der PH-Rehabilitation

- Entwicklung von Parametern zur besseren Bemessung von Aktivität und Partizipation
- Evaluation von Teilkomponenten PAH-Rehabilitation
- Gruppentherapie/Erfahrungsaustausch für PAH-Patienten ausbauen

BARMELWEID

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