

Protocol for cycle exercise training (table S1). Protocol based on a previous trial investigating exercise training in lung transplantation waitlist patients [1].

Table S1 Exercise training protocol for endurance cycle training [1]

Time	Duration
1. Week – Day 1	1x 10 minutes
1. Week – Day 2	1x 11 minutes
1. Week – Day 3	1x 12 minutes
1. Week – Day 4	1x 13 minutes
1. Week – Day 5	1x 14 minutes
2. Week – Days 1-5	1x 20 minutes
3. Week – Day 1	1x 22 minutes
3. Week – Day 2	1x 24 minutes
3. Week – Day 3	1x 26 minutes
3. Week – Day 4	1x 28 minutes
3. Week – Day 5	1x 30 minutes

Pre- and post-PR values of all outcomes for both groups.

Table S2 Exercise capacity and quality of life measures at pre and post pulmonary rehabilitation (PR)

	Pre-PR		Post-PR	
	Control-group	HI-NIV group	Control-group	HI-NIV group
CET				
Time s	283±163	262±184	424±233	508±400
HADS pts				
Anxiety	7.7±5.1	10.6±5.9	7.3±4.7	8.6±4.2
Depression	4.7±2.7	6.3±4.1	4.8±3.1	5.7±3.3
SRI pts				
Summary scale	45.6±11.3	54.5±4.5	46.2±9.1	51.1±8.0
CRQ pts				
Total score	4.1±1.1	3.5±0.9	4.5±0.9	4.5±1.1
Dyspnoea	3.3±1.0	2.6±0.9	3.5±1.1	3.4±1.2
Fatigue	4.3±1.2	3.5±1.1	4.7±1.0	4.5±1.2
Emotional Function	4.5±1.2	3.7±1.2	4.9±1.1	4.9±1.2
Mastery	4.3±1.5	3.9±1.1	4.8±1.3	4.9±1.1
6MWT				
Distance m	228±101	237±121	269±90	287±137
Knee extension peak force				
N	249±110	247±136	269±108	273±146
% pred ^[2]	77±25	70±16	85±25	77±15

Data presented as mean and standard deviation. CET: cycle endurance test; HADS: hospital anxiety and depression scale; SRI: severe respiratory insufficiency questionnaire; CRQ: chronic respiratory disease questionnaire; 6MWT: 6-minute walk test.

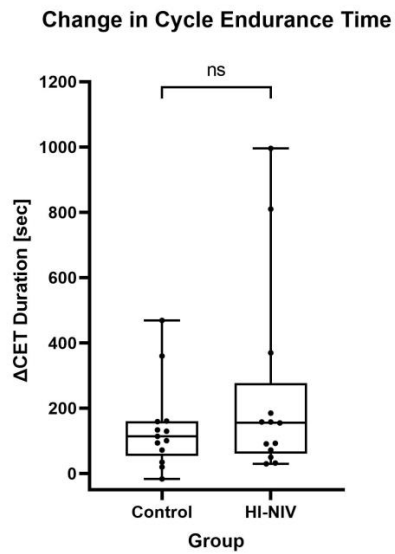


Figure S1. Pre- to post pulmonary rehabilitation changes in cycle endurance time. n.s.= not significant.

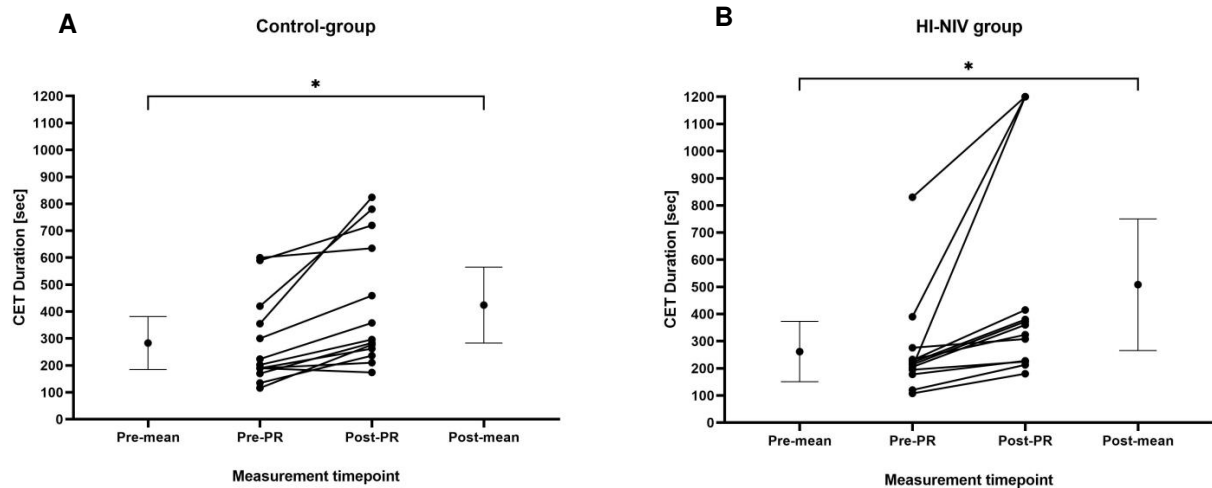


Figure S2. Individual pre- to post pulmonary rehabilitation (PR) changes of cycle endurance time; A: presenting control-group, B: presenting high-intensity non-invasive ventilation group (HI-NIV). *: significant within-group difference from pre-PR.

Table S3 Physiological response during the cycle endurance test at end exercise of the pre pulmonary rehabilitation (PR) test and at isotime (identical workload) of the post PR cycle endurance test: within-group and between-group statistical analyses

	Control-group (n=13)			HI-NIV group (n=13)			Between-group difference (HI-NIV group – control-group)	
	Pre-PR end- exercise	Post-PR isotime	Difference	Pre-PR end- exercise	Post-PR isotime	Difference	Mean difference	p-value
PaCO₂ mmHg	60.3±7.8	59.8±6.9	-0.5 [-5.3 to 4.3]	60.2±5.6	56.5±6.4	-3.7 [-6.6 to -0.8]*	-3.2 [-8.4 to 1.9]	0.214
pH	7.30±0.05	7.30±0.05	0.0 [-0.02 to 0.03]	7.30±0.03	7.32±0.03	0.02 [0 to 0.04]*	0.02 [-0.01 to 0.04]	0.111
Lactate mmol/l	2.9±1.9	2.7±1.4	-0.2 [-0.6 to 0.1]	2.9±0.9	2.8±0.9	-0.1 [-0.5 to 0.3]	0.1 [-0.34 to -0.71]	0.475
PaO₂ mmHg	63.7±14.0	67.5±19.7	3.8 [-3.0 to 10.6]	70.8±14.5	70.0±15.3	-0.8 [-5.3 to 3.7]	-4.6 [-12.2 to 3.2]	0.224
Blood pressure								
systolic mmHg	153±26	156±18	3 [-14 to 21]	161±20	149±19	-12 [-20 to -3]*	-15.0 [-34.3 to 2.8]	0.092
diastolic	83±11	85±11	2 [-6 to 11]	90±14	88±10	-2 [-8 to 4]	-4.0 [-14.6 to 5.4]	0.350
RR breaths/ min⁻¹	26.1±10.9	26.6±12.3	0.5 [-1.2 to 2.2]	23.3±4.0	25.4±7.1	2.1 [-2.0 to 6.2]	1.6 [-2.1 to 5.3]	0.37
HR beats/ min⁻¹	107.3±14.2	102.7±15.8	-4.6 [-12.1 to 3.0]	108.5±12.6	106.3±11.6	-2.2 [-10 to 5.8]	2.4 [-8.0 to 12.8]	0.64
Dyspnoea pts	6.4±1.4	6.0±1.3	-0.4 [-1.2 to 0.4]	6.7±1.3	4.3±1.8	-2.4 [-3.4 to -1.4]*	-2.0 [-3.2 to -0.8]	0.005**
Respiratory effort pts	5.9±1.3	5.8±1.6	-0.1 [-0.9 to 0.8]	6.7±2.0	4.8±2.2	-1.9 [-3.2 to -0.6]*	-1.8 [-3.3 to -0.4]	0.022**
Leg fatigue pts	4.4±1.6	3.7±1.8	-0.7 [-1.6 to 0.2]	5.5±2.3	3.8±1.5	-1.7 [-3.3 to -0.1]	1.0 [-2.8 to 0.8]	0.419

Data presented as mean±standard deviation and as mean [95% CI]. PaCO₂: partial pressure of carbon dioxide; ph: potential of hydrogen; PaO₂: partial pressure of oxygen; RR: respiratory rate; HR: heart rate; *: significant within-group difference from pre-PR; **: significant between-group difference.

Table S4. Average settings and measurements of high-intensity NIV during exercise training program in the HI-NIV group**Settings**

Subjects	13
IPAP cmH ₂ O	26.0±3.5
EPAP cmH ₂ O	5.7±0.8
TI s	0.9±0.09
RR breaths/ min ⁻¹	21.4±2.7

Measurements

Tidal volume mL	1108±261
Minute ventilation mL	23±5
TI/Ttotal %	32.0±2.6
Proportion of mandatory mechanical breaths %	86±10

Data presented as mean±SD. IPAP: inspiratory positive airway pressure; EPAP: expiratory positive airway pressure; TI: inspiratory time; RR: respiratory-rate; TI/Ttotal: Inspiratory time/total inspiratory and expiratory time ratio.

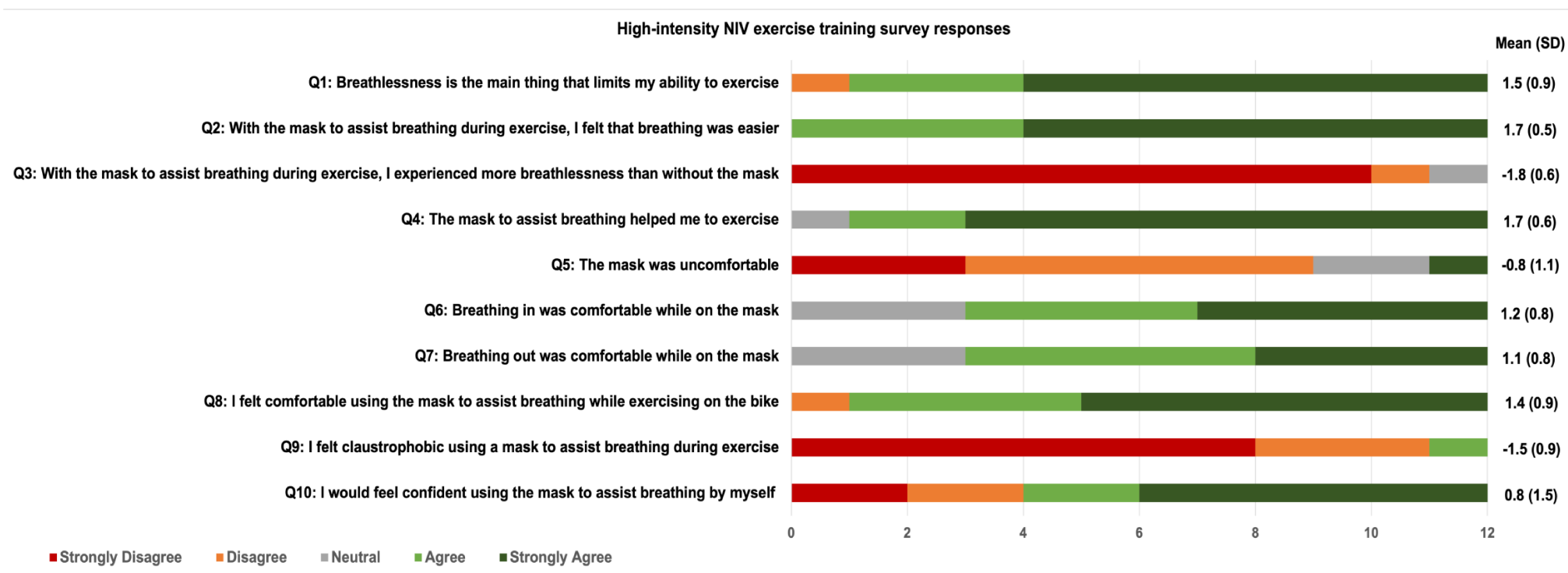


Figure S3. Post-NIV exercise training survey responses (n=12). Mean and SD calculated from scored responses. Responses scored as: strongly agree=2; agree=1; neutral=0; disagree= -1; strongly disagree= -2.

Post-hoc power analysis: cycle endurance time in people with very severe COPD and chronic hypercapnic respiratory failure treated with nocturnal non-invasive ventilation.

Table S5 Post-hoc power analysis

An a posteriori power calculation based upon the data from the current trial showed that group sample sizes of n=56 in both groups (HI-NIV group & control-group) achieve 82% power to detect a difference of 105 seconds at the 5% level using a one-sided Welch t-Test.

Literature

1. Gloeckl R, Halle M, Kenn K. Interval versus continuous training in lung transplant candidates: a randomized trial. *J Heart Lung Transplant* 2012; 31(9): 934-941.
2. Andrews AW, Thomas MW, Bohannon RW. Normative values for isometric muscle force measurements obtained with hand-held dynamometers. *Phys Ther* 1996; 76(3): 248-259.