

Online Supplementary Material

Low-load blood-flow restriction strength training in patients with COPD:

a randomised single-blind pilot study

Dario Kohlbrenner^{1,2}, Manuel Kuhn^{1,2}, Anastasios Manettas^{3,4}, Céline Aregger³, Matthias Peterer³, Nicola Greco³, Noriane A. Sievi², Christian F. Clarenbach^{1,2}

¹Faculty of Medicine, University of Zurich, Zurich, Switzerland

²Department of Pulmonology, University Hospital Zurich, Zurich, Switzerland

³Physiotherapy Occupational Therapy, University Hospital Zurich, Zurich, Switzerland

⁴Biomechanics and Ergonomics, ErgoMech Laboratory, Department of Physical Education and Sport Science, University of Thessaly, Trikala, Greece

Corresponding author:

Dario Kohlbrenner, PhD
University Hospital Zurich
Department of Pulmonology
Rämistrasse 100
8091 Zurich
Switzerland
dario.kohlbrenner@usz.ch

Methods

Participants were asked to refrain from exercise and strenuous activities for the 24h preceding the visits. In addition, they were asked to avoid intake of caffeine and heavy meals 4h before the visits.

Secondary outcomes

We used the 3-8 repetition maximum (RM) test [1], performed after a warm-up procedure (i.e., 15 repetitions with a weight estimated to be approximately 50% of the individual 1-RM). For the test, participants performed as many technically correct and full range of motion repetitions as possible. If muscular failure in the first set of testing did not occur within 3-8 repetitions, an additional set was carried out after 5min of rest. No more than three sets of testing were done to ensure reproducible values. The 1-RM was estimated using the equation:

$$1\text{-RM predicted} = \frac{\text{weight lifted}}{1.0278 - 0.0278 \times \text{the number of repetitions performed}}$$

Results were recorded in kilograms. The results of this test were also used to set the initial exercise training loads.

Functional exercise capacity was measured with the 6-minute walk test (6MWT) according to American Thoracic Society / European Respiratory Society (ATS/ERS) technical standards [2], and the 1-minute sit-to-stand test (1MSTST), which is a valid and reliable test in COPD [3].

Cardiopulmonary exercise testing (CPET) was performed in accordance with published ERS standards [4]. We used a bicycle ergometer (ergoselect33 100, ergoline GmbH, Sitz, Germany) with an incremental ramp protocol (initial load 20W +10W/min for women and 30W +10W/min for men). Respiratory parameters were collected breath-by-breath (Ergostik, Geratherm Respiratory GmbH, Bad Kissingen, Germany).

Lung function was measured according to ATS/ERS technical standards [5, 6].

Physical activity (PA) was recorded with a triaxial accelerometer of a multisensory activity monitor (SenseWear Pro, Bodymedia Inc., Pittsburgh, PA, USA). We used the number of steps per day as an indicator for PA. The device was worn as an armband on the left upper arm for seven days, around the clock except during water-based activities (e.g., showering, swimming). Days with a minimum of 22.5h on-body time were considered valid days [7]. Over the 7-day assessment period, a minimum of four valid recording days were required to include PA data for final analysis [7]. Minimal clinical important differences (MCIDs) reported for PA in COPD populations are relatively broad (i.e., between 350 and 1100 steps/day) [8]. We applied a rather high threshold of 1000 steps/day to our analysis.

Participants were asked to complete a number of questionnaires. We assessed symptom

burden with the COPD Assessment test (CAT), a valid and reliable questionnaire specifically designed for the COPD population [9]. The MCID of the CAT is considered -2 points [10]. We assessed health-related quality-of-life (HrQoL) with the Chronic Respiratory Questionnaire (CRQ) and the Short-Form-12 (SF-12). While the CRQ is specifically designed for chronic respiratory disease populations, the SF-12 is generically targeting HrQoL [11, 12]. The MCID for the CRQ is 0.5 points for the dyspnoea, fatigue, emotion, and mastery subscales [13]. The MCID for the SF-12 is 3 points in the physical component subscale (PCS), and 3.5 points in the mental component subscale [14]. Depression and anxiety symptoms were assessed with the Hospital Anxiety and Depression Scale (HADS), a valid and reliable questionnaire in the COPD population [15]. The HADS consists of an Anxiety and a Depression subscale, the MCID is considered -1.5 points in both [15]. Finally, participants were asked to fill a purpose-designed questionnaire at the end of their study participation (see below for the original and a translated version of the questionnaire).

Results

Lower limb arterial occlusion pressure

AOPs in the LL-BFRT group were 154 (43), 149 (38), 143 (33), and 162 (27) mmHg at the first, 8th, 16th training, and follow-up, respectively. AOPs in the HL-ST group were 172 (28), 168 (24), 159 (25), and 167 (29) mmHg at the first, 8th, 16th training, and follow-up, respectively.

Purpose-designed questionnaire (original)

Fragebogen zum Abschluss der Studie LL-BFRT in COPD

Inwiefern hat sich Ihre körperliche Leistungsfähigkeit während der Studie verändert?

1	2	3	4	5	6	7	8	9	10
Hat stark abgenommen				Gleich geblieben					Hat sich stark verbessert

Wie anstrengend empfanden Sie das Krafttraining durchschnittlich?

1	2	3	4	5	6	7	8	9	10
Überhaupt nicht anstrengend									Extrem anstrengend

Hatten Sie Muskelkater aufgrund des Trainings in der ambulanten pulmonalen Rehabilitation?

1	2	3	4	5	6	7	8	9	10
Nie				Mässiger Muskelkater					Extremer Muskelkater

Purpose-designed questionnaire (translated from German)

Questionnaire to conclude your study participation

How did your physical fitness change during the study?

1	2	3	4	5	6	7	8	9	10
Strongly declined				Unchanged					Strongly improved

How hard did you perceive the exercise training on average?

1	2	3	4	5	6	7	8	9	10
Not exhausting at all									Extremely exhausting

Did you have muscle soreness from the exercise training? How intense did it feel?

1	2	3	4	5	6	7	8	9	10
Never				Moderate muscle soreness					Extreme muscle soreness

Supplementary Figures

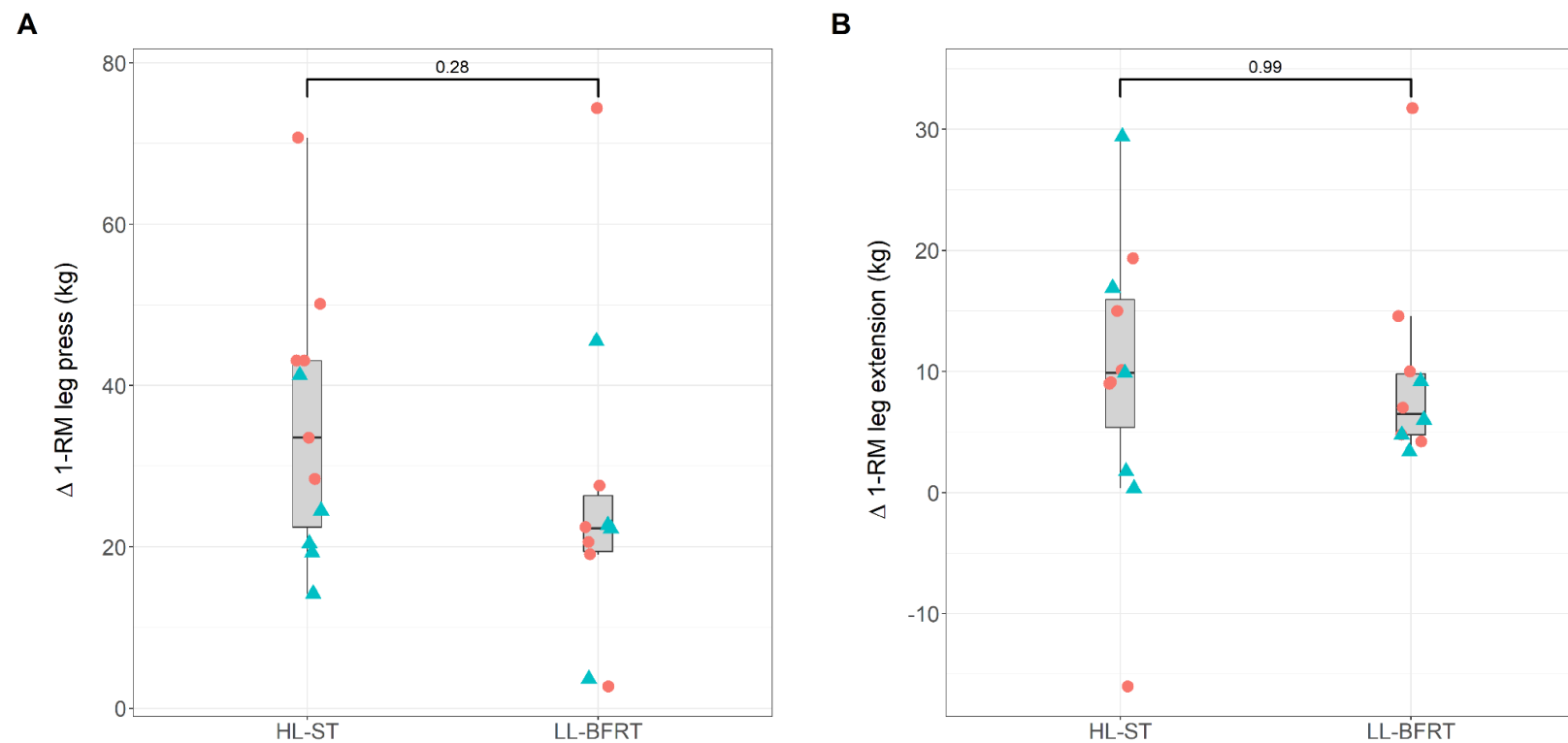


Figure S1. Changes in estimated 1-RM stratified by group. A, leg press; B, leg extension. Individual data is stratified for females (blue triangles) and males (red circles). Δ , change post-pre study intervention; 1-RM, 1-repetition maximum; kg, kilogram; HL-ST, high-load strength training; LL-BFRT, low-load blood-flow restriction training.

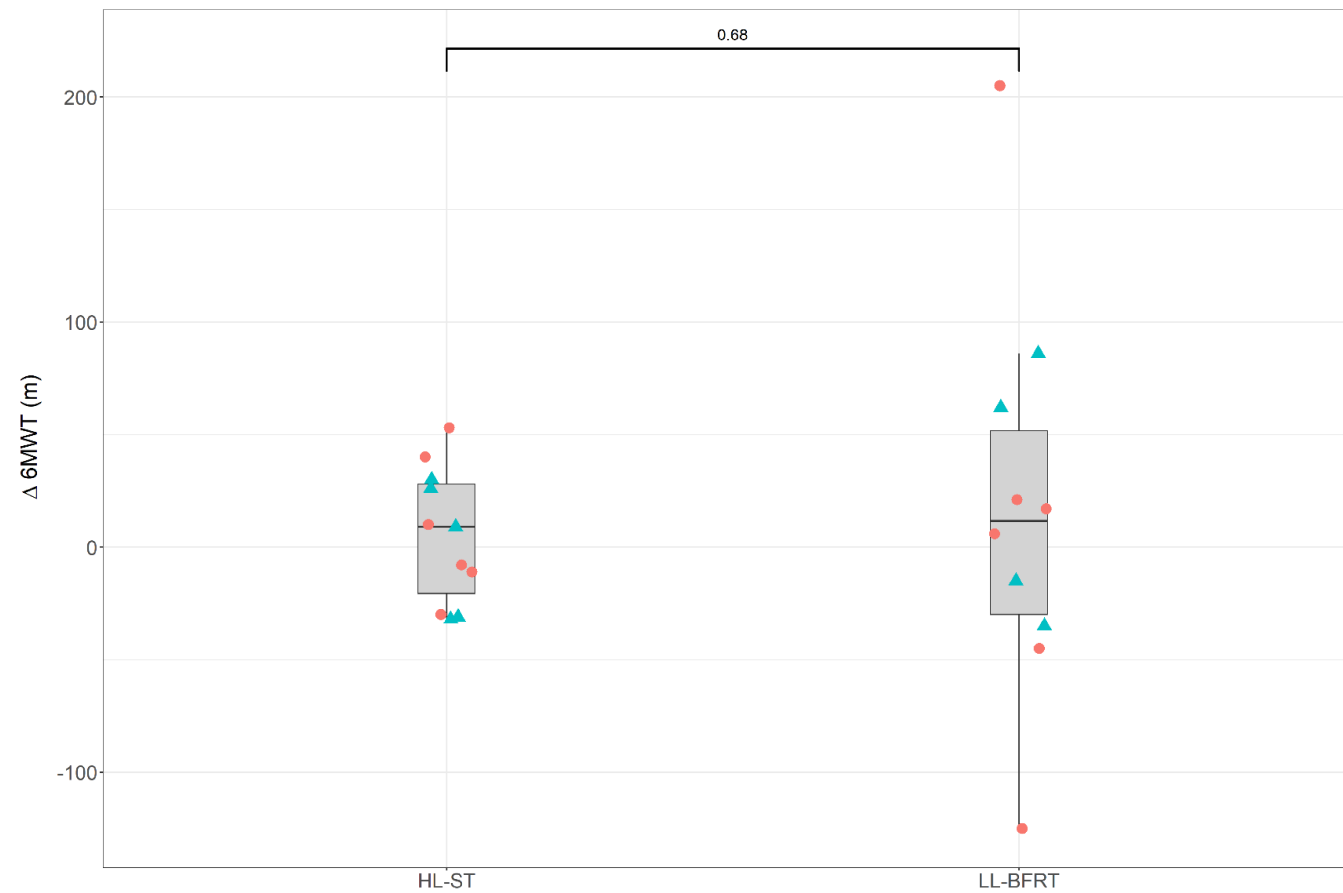


Figure S2. Changes in 6MWT distance stratified by group. Individual data is stratified for females (blue triangles) and males (red circles). Δ , change post-pre study intervention; 6MWT, 6-minute walk test; m, meters; HL-ST, high-load strength training; LL-BFRT, low-load blood-flow restriction training.

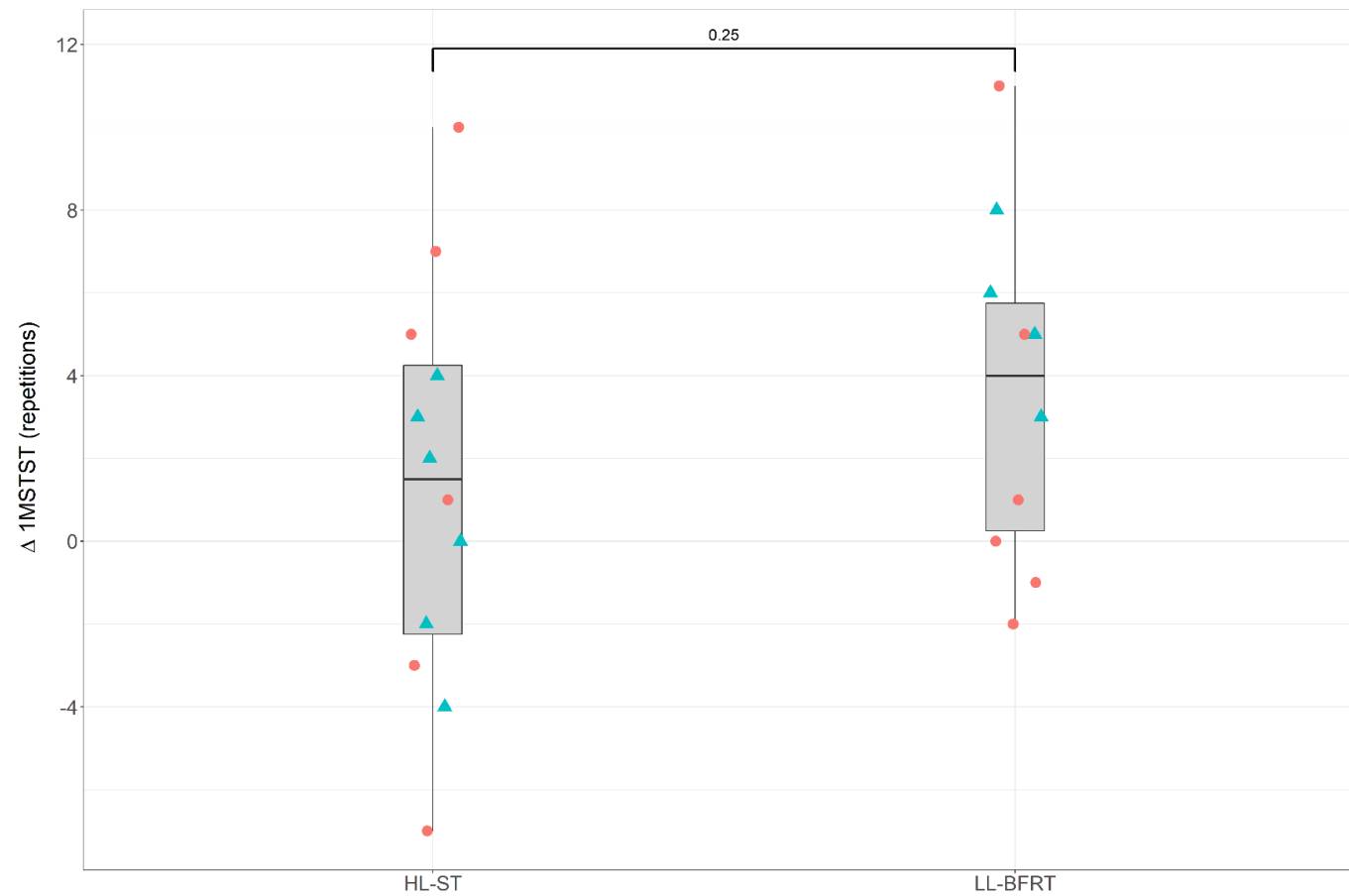


Figure S3. Changes in 1MSTST stratified by group. Individual data is stratified for females (blue triangles) and males (red circles). Δ , change post-pre study intervention; 1MSTST, 1-minute sit-to-stand test; HL-ST, high-load strength training; LL-BFRT, low-load blood-flow restriction training.

References

1. Brzycki M. Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue. *Journal of Physical Education, Recreation & Dance* 1993; 64(1): 88-90.
2. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, McCormack MC, Carlin BW, Sciurba FC, Pitta F, Wanger J, MacIntyre N, Kaminsky DA, Culver BH, Revill SM, Hernandez NA, Andrianopoulos V, Camillo CA, Mitchell KE, Lee AL, Hill CJ, Singh SJ. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J* 2014; 44(6): 1428-1446.
3. Crook S, Busching G, Schultz K, Leibert N, Jelusic D, Keusch S, Wittmann M, Schuler M, Radtke T, Frey M, Turk A, Puhan MA, Frei A. A multicentre validation of the 1-min sit-to-stand test in patients with COPD. *Eur Respir J* 2017; 49(3).
4. Radtke T, Crook S, Kaltsakas G, Louvaris Z, Berton D, Urquhart DS, Kampouras A, Rabinovich RA, Verges S, Kontopidis D, Boyd J, Tonia T, Langer D, De Brandt J, Goertz YMJ, Burtin C, Spruit MA, Braeken DCW, Dacha S, Franssen FME, Laveneziana P, Eber E, Troosters T, Neder JA, Puhan MA, Casaburi R, Vogiatzis I, Hebestreit H. ERS statement on standardisation of cardiopulmonary exercise testing in chronic lung diseases. *Eur Respir Rev* 2019; 28(154): 180101.
5. Graham BL, Brusasco V, Burgos F, Cooper BG, Jensen R, Kendrick A, MacIntyre NR, Thompson BR, Wanger J. 2017 ERS/ATS standards for single-breath carbon monoxide uptake in the lung. *Eur Respir J* 2017; 49(1).
6. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, Kaminsky DA, McCarthy K, McCormack MC, Oropez CE, Rosenfeld M, Stanojevic S, Swanney MP, Thompson BR. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am J Respir Crit Care Med* 2019; 200(8): e70-e88.
7. Watz H, Pitta F, Rochester CL, Garcia-Aymerich J, ZuWallack R, Troosters T, Vaes AW, Puhan MA, Jehn M, Polkey MI, Vogiatzis I, Clini EM, Toth M, Gimeno-Santos E, Waschki B, Esteban C, Hayot M, Casaburi R, Porszasz J, McAuley E, Singh SJ, Langer D, Wouters EF, Magnussen H, Spruit MA. An official European Respiratory Society statement on physical activity in COPD. *Eur Respir J* 2014; 44(6): 1521-1537.
8. Teylan M, Kantorowski A, Homsy D, Kadri R, Richardson C, Moy M. Physical activity in COPD: Minimal clinically important difference for medical events. *Chronic respiratory disease* 2019; 16: 1479973118816424.
9. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. *Eur Respir J* 2009; 34(3): 648-654.

10. Kon SS, Canavan JL, Jones SE, Nolan CM, Clark AL, Dickson MJ, Haselden BM, Polkey MI, Man WD. Minimum clinically important difference for the COPD Assessment Test: a prospective analysis. *The Lancet Respiratory medicine* 2014; 2(3): 195-203.
11. Wijkstra PJ, TenVergert EM, Van Altena R, Otten V, Postma DS, Kraan J, Koeter GH. Reliability and validity of the chronic respiratory questionnaire (CRQ). *Thorax* 1994; 49(5): 465-467.
12. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; 34(3): 220-233.
13. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials* 1989; 10(4): 407-415.
14. Jones PW, Brusselle G, Dal Negro RW, Ferrer M, Kardos P, Levy ML, Perez T, Soler-Cataluna JJ, van der Molen T, Adamek L, Banik N. Health-related quality of life in patients by COPD severity within primary care in Europe. *Respiratory medicine* 2011; 105(1): 57-66.
15. Nikolovski A, Gamgoum L, Deol A, Quilichini S, Kazemir E, Rhodenizer J, Oliveira A, Brooks D, Alsubheen S. Psychometric properties of the Hospital Anxiety and Depression Scale (HADS) in individuals with stable chronic obstructive pulmonary disease (COPD): a systematic review. *Disability and rehabilitation* 2023: 1-9.