Improvements in functional and cognitive status following a short-term pulmonary rehabilitation in COPD lung-transplant recipients – A pilot study

Online Data Supplement

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Neuropsychological Testing battery

A comprehensive neuropsychological assessment battery was used for the LTx-recipients cognitive assessment including the following clinical tools in German version on PR admission and at discharge: 1) Wechsler Memory Scales IV: Logical Memory I [LG1], Logical Memory II [LG2] [1], 2) California Verbal Learning Test (CVLT): word learning [LS], reading section 1 [DG1], reading section 5 [DG5], word list for interference effect [LB], delayed free repetition [VFW], repetition with help [WA], and repetition errors [W] [2]; 3) Test battery of attentional performance (TAP): Index of Speed- Accuracy- Trade off [ISAT %], Divided attention performance [GAA %] [3]; 4) Trail Making Test (TMT): Test version A [TMT-A sec], Test version B [TMT-B sec] [4]; 5) Stroop test - colour word interference: colour-word read [FWL], colour recognition [FSB], interference performance [INT] [5]; 6) Behavioural Assessment of the Dysexecutive Syndrome (BADS test): Test version A [BV-1], Test version B [BV-2] [6]; 7) Clock-drawing test [7] (Please see Figure 1 and online supplement for more details). Multiple scores achieved in the administered cognitive tests determined the evaluation of cognitive performance for the following domains: a) Memory ability, b) Learning skills, c) Attention and flexibility, d) Psychomotor speed, e) Behavioural activation, f) Visuospatial and processing speed, and g) Visuospatial and praxis. One composite score for each of the cognitive domains was calculated by adding all the mean achieved scores from the cognitive tests that correspond to certain cognitive domains (Online table 3).

Six-minute walk test

The 6MWT was performed according to international recommendations [8, 9]. Briefly, participants were asked to walk indoors on a flat, straight, 30-meter walking course as far as they can under the supervision of a well-trained researcher. Blood oxygen saturation (SpO₂), dyspnea and leg-fatigue (Borg-scale) were assessed. Distance-saturation product (DSP) was calculated as the product of the final distance walked in meters and the post-exercise SpO₂% (DSP m% = 6MWD m × SpO₂%post /100) [10]. Unintended stop points were defined as a (temporary) discontinuation of the 6MWT [11].
### Supplementary tables

**Online table 1. Cognitive tests categorized based on the evaluation of different cognitive domains**

| Memory ability | Learning skills | Attention & flexibility | Psychomotor speed |
|----------------|-----------------|-------------------------|-------------------|
| Wechsler Memory Scales IV: [LG1] | California Verbal Learning Test: [LS1] | Test battery of Attentional Performance: [ISAT1] | Stroop test – colour-word interference: [FWL] |
| Wechsler Memory Scales IV: [LG2] | California Verbal Learning Test: [DG1] | Test battery of Attentional Performance: [GAAP1] | Stroop test – colour-word interference: [FSB] |
| California Verbal Learning Test: [VFW1] | California Verbal Learning Test: [DG5] | Stroop test – colour-word interference: [INT] |
| California Verbal Learning Test: [VFW2] | California Verbal Learning Test: [LB] |                      |                   |
| California Verbal Learning Test: [WA1] |                      |                      |                   |
| California Verbal Learning Test: [WA2] |                      |                      |                   |
| California Verbal Learning Test: [W] |                      |                      |                   |
| Behavioural activation | Visuospatial & processing speed | Visuospatial & praxis ability |                      |
| Behavioural Assessment of the Dysexecutive Syndrome: [BADS- BV1] | Trail Making Test: [TMT-A] | Clock-Drawing Test: [Uhr-Test] |                      |
| Behavioural Assessment of the Dysexecutive Syndrome: [BADS- BV2] | Trail Making Test: [TMT-B] |                      |                      |

**Online table 1**: Domain-specific cognitive evaluation was performed using these test for each cognitive domain. The sum of the scores in these cognitive tests determined the *composite score* for each corresponding cognitive domain. Within brackets are the abbreviations for the *German version* of the performed cognitive tests.
**Online table 2. A single-day exercise training in Pulmonary Rehabilitation program**

| **Endurance training**          | **Duration** | **Intensity**          |
|---------------------------------|--------------|------------------------|
| Bicycle ergometer               | 20 minutes   | 70% of peak work rate  |

**Strength training**

| Activity                        | **Repetitions** | **Intensity**                      |
|---------------------------------|-----------------|------------------------------------|
| Leg press                       |                 |                                    |
| Knee extension                  |                 |                                    |
| Hip abduction/adduction         | 3 set X         | Individual load is set to reach momentary muscular failure at the end of each set |
| Shoulder Pull Down              | 15 repetitions  |                                    |
| Rowing                          |                 |                                    |
| Abdominal muscles               |                 |                                    |

*Estimated duration: 30 minutes*

**Activities of daily living training**

| Activity                                      | **Duration** | **Intensity**                      |
|-----------------------------------------------|--------------|------------------------------------|
| walking training and/or calisthenics exercises using body weight, small dumb-bells, rubber tubes etc. | 30 minutes   | Low to moderate individual exertion |

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**Online table 2:** Elements of the exercise training of the implemented 3-week PR program in LTx-recipients for COPD.
Online table 3. Pearson’s correlations amongst cognitive tests performance and health and mental status

| Memory ability          | HADS Anxiety | HADS Depression | CRQ Dyspnea | CRQ Fatigue | CRQ Emotion | CRQ Mastery |
|-------------------------|--------------|-----------------|-------------|-------------|-------------|-------------|
| WMS Logical Memory I    | 0.11         | -0.09           | 0.19        | 0.01        | 0.01        | 0.05        |
| WMS Logical Memory II   | 0.07         | 0.12            | 0.17        | -0.06       | 0.04        | -0.02       |
| CVLT Free recall – list 1 | 0.42         | -0.37           | 0.10        | 0.08        | 0.19        | 0.21        |
| CVLT Free recall – list 2 | -0.44        | -0.16           | 0.22        | 0.25        | 0.30        | 0.30        |
| CVLT Recall with help- List 1 | -0.36        | -0.08           | 0.48        | 0.26        | 0.47        | 0.43        |
| CVLT Recall with help- List 2 | -0.62**      | -0.43           | 0.47        | 0.26        | 0.42        | 0.40        |
| CVLT Repeating errors   | -0.06        | -0.48           | -0.22       | -0.08       | -0.16       | -0.02       |

| Learning skills         |              |                 |             |             |             |             |
| CVLT Learning ability, %| -0.46        | -0.19           | 0.22        | 0.15        | 0.25        | 0.22        |
| CVLT Passage 1, %       | -0.24        | 0.05            | -0.04       | 0.14        | 0.24        | 0.24        |
| CVLT Passage 5, %       | -0.52*       | -0.43           | 0.47        | 0.34        | 0.34        | 0.38        |
| CVLT List B, %          | 0.02         | 0.33            | 0.03        | 0.07        | 0.18        | 0.11        |

| Attention & Flexibility |              |                 |             |             |             |             |
| TAP Speed / accuracy, %  | 0.26         | -0.16           | -0.44       | -0.37       | -0.15       | -0.28       |
| TAP Shared attention, %  | 0.13         | 0.17            | -0.04       | 0.01        | -0.02       | 0.11        |

| Visuospatial & processing |              |                 |             |             |             |             |
| TMT - A, score           | 0.46         | 0.15            | -0.27       | -0.25       | -0.20       | -0.17       |
| TMT - B, score           | 0.06         | -0.02           | -0.33       | -0.31       | -0.29       | -0.15       |

| Visuospatial & praxis ability |              |                 |             |             |             |             |
| CDT Clock test            | 0.30         | 0.29            | -0.18       | -0.03       | -0.03       | -0.12       |

| Psychomotor Speed         |              |                 |             |             |             |             |
| Stroop colour-word read   | -0.22        | 0.27            | 0.29        | 0.23        | 0.24        | 0.15        |
| Stroop colour recognition | -0.45        | -0.23           | 0.50*       | 0.28        | 0.24        | 0.27        |
| Stroop interference       | -0.03        | 0.11            | 0.11        | -0.03       | -0.11       | -0.06       |

| Behavioural activation    |              |                 |             |             |             |             |
| BADS version 1            | 0.21         | 0.17            | 0.09        | -0.22       | -0.32       | -0.28       |
| BADS version 2            | 0.32         | 0.21            | 0.21        | 0.26        | 0.19        | 0.22        |

**Online table 3**: Pearson’s correlations ($r$) amongst cognitive, mental, and health status tests. Asterisks denote significance (* $p<0.05$, ** $p<0.001$).
Online table 4: Differences in clinical characteristics after stratification by single- and bilateral- LTx. Data are mean ± SD unless specified otherwise. Level of significance was set at $P \leq 0.05$. 

| Clinical characteristics | All Patients (n=24) | Single-LTx (n=8, 33%) | Double-LTx (n=16, 67%) | P Value |
|--------------------------|---------------------|-----------------------|------------------------|---------|
| Women, n, (%)            | 10 (42)             | 3 (37)                | 7 (44)                 | NS      |
| Age, years, ±SD          | 58.2 ±6.3           | 62.4 ±4.7             | 56.1 ±6.1              | 0.019   |
| Height, m                | 1.71 ±0.09          | 1.74 ±0.08            | 1.70 ±0.09             | NS      |
| Weight, kg               | 64.6 ±12.1          | 64.7 ±12.7            | 64.5 ±12.4             | NS      |
| BMI kg·m⁻²               | 22.0 ±3.5           | 21.5 ±4.0             | 22.2 ±3.4              | NS      |
| FEV₁, %pred.             | 75.4 ±22.0          | 54.3 ±10.4            | 86.6 ±17.8             | <0.001  |
| DLCO, %                  | 53.5 ±16.4          | 38.3 ±8.5             | 58.6 ±16.4             | 0.019   |
| RV/TLC, %                | 55.6 ±12.1          | 66.3 ±3.7             | 49.9 ±11.1             | <0.001  |
| CRQ dyspnea, score       | 4.7 ±2.1            | 4.3 ±1.9              | 5.0 ±2.3               | NS      |
| CRQ fatigue, score       | 4.9 ±1.5            | 4.9 ±1.6              | 4.9 ±1.5               | NS      |
| CRQ emotion, score       | 5.5 ±1.4            | 5.4 ±1.3              | 5.6 ±1.6               | NS      |
| CRQ mastery, score       | 5.8 ±1.4            | 5.6 ±1.6              | 6.0 ±1.4               | NS      |
| HADS anxiety, score      | 4.4 ±4.2            | 4.4 ±3.6              | 4.4 ±4.7               | NS      |
| HADS depression, score   | 3.8 ±3.5            | 4.9 ±4.6              | 3.1 ±2.5               | NS      |
| Education, years         | 8.0 ±2.6            | 7.9 ±2.7              | 8.1 ±2.6               | NS      |
| IQ, score                | 110.0 ±12.4         | 109.1 ±11.3           | 110.4 ±13.2            | NS      |
| 6MWD, m                  | 346 ±127            | 321 ±152              | 349 ±122               | NS      |
| 6MWD, %pred.             | 51.0 ±17.7          | 51.8 ±17.4            | 50.6 ±18.5             | NS      |
| DSP, m%                  | 326 ±124            | 299 ±146              | 333 ±115               | NS      |
| Unintended stop point, m | 340 ±130            | 321 ±153              | 349 ±122               | NS      |
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