SUPPLEMENTARY DATA

# Title: Impact of cardiovascular and metabolic comorbidities on long-term outcomes of home-based pulmonary rehabilitation in COPD

# Short title: COPD comorbidities and pulmonary rehabilitation

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**Supplementary Table 1 Patients reported other comorbidities**

|  |  |
| --- | --- |
|  | **Whole population****(n=419)** |
| **Anxiety-depression (n, %)** | 182 (43.4) |
|  - Anxiety | 147 (35.1) |
|  - Depression | 92 (22) |
| **Respiratory diseases (n, %)** | 185 (44.2) |
|  - Obstructive sleep apnea syndrome | 83 (19.8) |
|  - Obesity hypoventilation syndrome | 30 (7.2) |
|  - Asthma | 20 (4.8) |
|  - Asbestosis | 8 (1.9) |
|  - Pneumoconiosis | 8 (1.9) |
| **Cancer (n, %)** | 54 (13) |
|  - History of lung cancer | 18 (4.4) |
| **Rheumatologic disease (n, %)** | 180 (42.9) |
| **Gastrointestinal disease (n, %)** | 109 (25.9) |
| **Neurological disease (n, %)** | 38 (9) |
| **Kidney disease (n, %)** | 32 (7.7) |
| **Thyroid disease (n, %)** | 31 (7.3) |

**Supplementary Table 2 Baseline description of patients who initiated PR according to availability for the M14 evaluation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  | **Reason for not****evaluated at M14** |
|  | **Evaluated M14****(n=303)** | **Not evaluated at M14** **(n=110)** | **ASD (%)** |  | **Dead****(n=36)** | **Loss of follow-up****(n=74)** |
| **Group** |  |  | 35.5 |  |  |  |
|  - Reference | 79 (26.1) | 23 (20.9) |  |  | 5 (13.9) | 18 (24.3) |
|  - Metabolic | 99 (32.7) | 23 (20.9) |  |  | 4 (11.1) | 19 (25.7) |
|  - Cardiovascular | 125 (41.3) | 64 (58.2) |  |  | 27 (75.0) | 37 (50.0) |
| **Age (years)** | 63.9 ± 11.1 | 64.5 ± 11.5 | 5.7 |  | 67.1 ± 9.2 | 63.3 ± 12.3 |
| **Male (n, %)** | 199 (65.7) | 75 (68.2) | 5.3 |  | 29 (80.6) | 46 (62.2) |
| **BMI (kg/m2)** | 27.6 ± 7.8 | 26.1 ± 7.3 | 19.9 |  | 24.5 ± 5.1 | 26.9 ± 8.1 |
|  - obesity (n, %) | 101 (33.6) | 26 (23.6) | 22.1 |  | 4 (11.1) | 22 (29.7) |
|  - underweight (n, %) | 60 (19.9) | 31 (28.2) | 19.4 |  | 9 (25.0) | 22 (29.7) |
| **Smoking status (n, %)** |  |  | 5.5 |  |  |  |
|  - current smoker | 40 (13.6) | 14 (13.0) |  |  | 5 (14.3) | 9 (12.3) |
|  - former smoker | 236 (80.3) | 89 (82.4) |  |  | 27 (77.1) | 62 (84.9) |
|  - never smoker | 18 (6.1) | 5 (4.6) |  |  | 3 (8.6) | 2 (2.7) |
| **Spirometry** |  |  |  |  |  |  |
|  - FEV1 (L) | 1.1 ± 0.5 | 0.9 ± 0.5 | 41.6 |  | 1.0 ± 0.5 | 0.9 ± 0.5 |
|  - FEV1 (% predicted) | 41.3 ± 17.1 | 33.0 ± 15.3 | 50.9 |  | 31.7 ± 16.9 | 33.5 ± 14.8 |
|  - FVC (L) | 2.2 ± 0.9 | 2.1 ± 0.8 | 16.6 |  | 1.8 ± 0.5 | 2.3 ± 0.9 |
|  - FVC (% predicted) | 65.2 ± 20.2 | 61.2 ± 18.2 | 23.0 |  | 54.3 ± 12.7 | 65.5 ± 19.9 |
|  - FEV1/FVC (%) | 50.5 ± 14.4 | 51.3 ± 14.3 | 5.4 |  | 49.7 ± 16.2 | 52.2 ± 13.3 |
| **COPD stages (n, %)** |  |  | 46.1\* |  |  |  |
|  - GOLD 1 | 2 (0.8) | 0 (0.0) |  |  | 0 (0.0) | 0 (0.0) |
|  - GOLD 2 | 62 (23.4) | 14 (16.1) |  |  | 4 (16.7) | 10 (15.9) |
|  - GOLD 3 | 124 (46.8) | 29 (33.3) |  |  | 5 (20.8) | 24 (38.1) |
|  - GOLD 4 | 77 (29.1) | 44 (50.6) |  |  | 15 (62.5) | 29 (46.0) |
| **Home ventilatory equipment (n, %)** |  |  |  |  |  |  |
|  - LTOT | 183 (60.4) | 88 (80.0) | 43.9 |  | 33 (91.7) | 55 (74.3) |
|  - NIV | 93 (30.7) | 45 (40.9) | 21.4 |  | 19 (52.8) | 26 (35.1) |
|  - CPAP | 25 (8.3) | 9 (8.2) | 0.3 |  | 2 (5.6) | 7 (9.5) |

**Notes:** Results are given as mean ± standard deviation for quantitative variables or frequencies (percentage) for categorical variables. Obesity and underweight are defined by BMI ≥ 30kg/m2 and ≤ 21kg/m2, respectively. \* due to too small Gold 1 size, Gold 1 and 2 were pooled together for the statistical analysis comparing patient repartitions between GOLD 1+2, GOLD 3 and GOLD 4. When the ASD less than 20%, the difference is considered negligible, between 20 and 50% the difference is small, between 50 and 80% it is medium and above 80% it is large.

**Abbreviations:** ASD, absolute standardized difference; BMI, body mass index; CPAP, continuous positive airway pressure; FEV1, forced expiratory volume in the first one second; FVC, forced vital capacity; GOLD, global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease; LTOT, long-term oxygen therapy; NIV, non-invasive ventilation.

**Supplementary Table 3 Exercise capacity, quality of life and anxiety-depression scores during follow-up for the whole population**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | M0 | M2 | M8 | M14 | p |
|
| **6MST** | 309 ±9 | 372 ±9 | 349 ±11 | 351 ±12 | <0.001 |
| **VSRQ** | 31.1 ±0.8 | 38.9 ±0.8 | 39.3 ±0.9 | 37.9 ±0.9 | <0.001 |
| **HAD** | 17.7 ±0.4 | 14.6 ±0.4 | 13.7 ±0.4 | 14.2 ±0.4 | <0.001 |
|  - HA | 9.7 ±0.2 | 8.5 ±0.2 | 7.9 ±0.2 | 8.1 ±0.2 | <0.001 |
|  - HD | 8.0 ±0.2 | 6.2 ±0.2 | 5.9 ±0.2 | 6.2 ±0.2 | <0.001 |

**Notes:** Evaluation of exercise capacity, quality of life and anxiety-depression performed before (M0), at the end (M2), and at 6 and 12 months after the end of PR (M8 and M14, respectively). Results are given as mean ± standard error for the whole population. p <0.05 are considered significant.

**Abbreviations:** 6MST, 6-minute stepper test (MCID 40); HAD, hospital anxiety and depression scale (MCID 1.5); HA, anxiety HAD subscore (MCID 1.5); HD, depression HAD subscore (MCID 1.5); VSRQ, visual simplified respiratory questionnaire (MCID 3.4).

**Supplementary Table 4 Baseline exercise capacity, quality of life and anxiety-depression for each group of patients**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Reference** | **Metabolic** | **Cardiovascular** | **p** |
| **6MST****(number of steps)** | 343 ±161 | 339 ±164 | 272 ±141 | <0.001 |
| **VSRQ****(score)** | 30.3 ±15.5 | 33.4 ±15.3 | 30.1 ±15.4 | 0.17 |
| **HAD****(score)** | 18.1 ±7.6 | 18.0 ±7.1 | 17.2 ±7.9 | 0.55 |
|  - HA | 9.8 ±4.5 | 10.3 ±4.2 | 9.3 ±4.8 | 0.19 |
|  - HD | 8.3 ±4.2 | 7.7 ±4.1 | 8.1 ±4.4 | 0.50 |

**Notes:** Basal evaluation of exercise capacity, quality of life and anxiety and depression assessed for all patients who beneficiated of an initial assessment. Results are given as mean ± standard deviation. p <0.05 are considered significant.

**Abbreviations:** 6MST, 6-minute stepper test; HAD, hospital anxiety and depression scale; HA, anxiety HAD subscore; HD, depression HAD subscore; VSRQ, visual simplified respiratory questionnaire.

**Supplementary Table 5 Sensitivity analysis: absolute variations of exercise capacity, quality of life and anxiety-depression for each group of patients, excluding underweight patients.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  **Reference****N = 51** | **Metabolic****N = 114** | **Cardiovascular****N = 159** | **p** |
| **6MST** |  |  |  |  |
|  M0 | 335 ±21 | 342 ±13 | 311 ±14 | 0.23 |
|  M2-M0 | 32 ±19 | 83 ±12 | 63 ±11 | 0.11 |
|  M8-M0 | 30 ±23 | 66 ±15 | 46 ±16 | 0.39 |
|  M14-M0 | 45 ±28 |  78 ±16 |  47 ±18 | 0.32 |
|  |  |  |  |  |
| **VSRQ** |  |  |  |  |
|  M0 | 29.9 ±2.4 | 33.9 ±1.5 | 32.3 ±1.5 | 0.36 |
|  M2-M0 | 9.4 ±2.3 | 8.5 ±1.4 | 7.0 ±1.3 | 0.89 |
|  M8-M0 | 7.9 ±2.4 | 9.5 ±1.6 | 8.4 ±1.5 | 0.46 |
|  M14-M0 | 6.8 ±2.6 | 8.0 ±1.7 | 6.0 ±1.6 | 0.45 |
|  |  |  |  |  |
| **HAD** |  |  |  |  |
|  M0 | 18.3 ±1.2 | 17.7 ±0.7 | 17.5 ±0.7 | 0.83 |
|  M2-M0 | -2.3 ±1.1 | -4.7 ±0.7 | -2.6 ±0.7 | 0.23 |
|  M8-M0 | -1.5 ±1.0 | -3.4 ±0.6 | -2.8 ±0.6 | 0.27 |
|  M14-M0 |  -3.1 ±1.1 | -4.7 ±0.6 $ |  -3.6 ±0.6 | 0.046 |
|  |  |  |  |  |
| **HA** |  |  |  |  |
|  M0 | 9.8 ±0.7  | 10.3 ±0.4 | 9.9 ±0.4 | 0.69 |
|  M2-M0 | -0.9 ±0.6 | -2.0 ±0.4 | -1.5 ±0.4 | 0.093 |
|  M8-M0 | -0.2 ±0.5 | -1.6 ±0.3 | -1.2 ±0.3 | 0.78 |
|  M14-M0 |  -1.5 ±0.7 |  -2.0 ±0.4 |  -1.6 ±0.4 | 0.34 |
|  |  |  |  |  |
| **HD** |  |  |  |  |
|  M0 | 8.7 ±0.7 | 7.4 ±0.4 | 7.6 ±0.4 | 0.31 |
|  M2-M0 | -1.4 ±0.7 | -2.8 ±0.4 | -1.1 ±0.4 | 0.65 |
|  M8-M0 | -1.3 ±0.6 | -1.8 ±0.3 | -1.5 ±0.3 | 0.094 |
|  M14-M0 |  -1.5 ±0.6 |  -2.8 ±0.4 $ |  2.0 ±0.4 | 0.013 |

**Notes:** Basal evaluation (M0) and evolutions of exercise capacity, quality of life and anxiety and depression assessed with the 6MST, VSRQ and HAD, respectively for each group of patients at the end of pulmonary rehabilitation (M2) and at 6 and 12 months after the end of PR (M8 and M14, respectively) and after exclusion of underweight patients (BMI ≤ 21 kg/m2). Results are adjusted to age, sex, BMI, FEV1 and LTOT status, and given as mean ± standard error. $ p < 0.05 when comparing Cartiovascular to Metabolic group. p < 0.05 are considered significant.

**Abbreviations:** 6MST, 6-minute stepper test; HAD, hospital anxiety and depression scale; HA, anxiety HAD subscore; HD, depression HAD subscore; VSRQ, visual simplified respiratory questionnaire.