**SUPPLEMTARY MATERIAL**

Protein supplementation combined with low-intensity resistance training in geriatric medical patients during and after hospitalization: a randomized, double-blind, multicenter trial

Josephine Gade, Anne Marie Beck, Hanne E. Andersen, Britt Christensen, Finn Rønholt, Tobias W. Klausen, Anders Vinther, Arne Astrup

**Supplementary Table 1.**

|  |
| --- |
| Grouping of participants according to amount of resistance training and physical activity\* |
|  | **Definition of Resistance training**† | **Definition of Physical Activity**‡ |
| **1: None/very little** | No/very little RT(≤ 6x RT in total during the 12 weeks) | Light physical activity < 2 hours/week |
| **2: Small amount/Little** | RT 1-2 x/week for 3-12 weeks (2-3 exercises, 2-3 sets) | Light physical activity 2-4 hours/week |
| **3: Moderate**  | RT 2-3 x/week for 6-12 weeks (2-3 exercises, 2-3 sets) | Light physical activity > 2 hours/week & moderate physical activity > 1 hour/week |
| **4: Regular**  | RT 3-4 x/week for 8-12 weeks (2-3 exercises, 2-3 sets) | Light physical activity > 4 hours/week or moderate physical activity 2-4 hours/week |
| **5: High amount**  | RT > 4 x/week for 8-12 weeks (2-3 exercises, 2-3 sets) | Moderate physical activity > 4 hours/week or hard physical activity > 2 hours/week |
| **\*** The grouping is based on a training/physical activity average for the entire period 12 weeks after discharge. † This category is only based on the amount of study resistance exercise training (RT) and possibly rehabilitation-training. During rehabilitation-training, one training session counts as one study RT-session. A RT-session only counts if minimum 2 exercises, ≥ 5 repetitions of 2 sets is performed (full session = 3 exercises, 10 repetitions of 3 sets). ‡Grouping adapted from Saltin & Grimby, Circulation 1968;38:1104-15. This category includes other training, e.g. swimming, golf, etc. and every day activities such as gardening, going for a walk, and house cleaning. |

**Supplementary Table 2.**

|  |
| --- |
| Baseline characteristics by treatment group\*  |
|  | **Protein** |  | **Placebo** | **N Protein/ Placebo** | **P-values** |
|  | **N** | **%** |  | **N** | **%** |
| Smokers | 8 | 11.0 |  | 3 | 4.0 | 73/75 | 0.107 |
| Alcohol overuse† | 8 | 11.0 |  | 7 | 9.3 | 73/75 | 0.743 |
| Cohabitant | 15 | 20.5 |  | 18 | 24.0 | 73/75 | 0.614 |
| Social contact‡ Every day 2-3 x/week 2-3 x/month < 2-3 x/month | 541423 | 74.019.22.74.1 |  | 512121 | 68.028.02.71.3 | 73/75 | 0.467 |
| Residence (admitted from) Own house/apartment Other§ | 685 | 93.26.8 |  | 741 | 98.71.3 | 73/75 | 0.114 |
| Chronic use of prednisolon | 4 | 5.5 |  | 4 | 5.3 | 73/75 | 1.000 |
| Vitamin D supplementation hospital Intake <19 µg/d & serum Vit. D < 50 nmol/L Intake >40 µg/d & serum Vit. D ≥ 100 nmol/L | 40 | 6.20.0 |  | 42 | 6.13.0 | 65/66 | 1.0000.496 |
| Vitamin D suppl. 12-weeks post discharge Intake <19 µg/d & serum Vit. D < 50 nmol/L Intake > 40 µg/d & serum Vit. D ≥100 nmol/L | 30 | 4.80.0 |  | 30 | 4.80.0 | 63/63 | 1.0001.000 |
| **Abbreviations;** Vit. D, 25-hydroxyvitamin D.\***Statistical tests:** Chi-square/Fisher’s exact test (counts < 5).†Defined as intakes > 7/14 unit/week (women/men).‡Includes relatives and friends, face to face or phone-calls.§ Includessheltered housing, nursing home, and rehabilitation facility. |

**Supplementary Table 3.**

|  |
| --- |
| Results for the primary and secondary endpoints, changes in performance between groups, Per-Protocol analysis\* |
|  | **Protein group**† | **Placebo group**† |  |
|  | **Baseline test**‡ | **Δ** **Baseline to discharge**§ | **Δ Discharge to 12 wk. after**  | **Δ** **Baseline to 12 wk. after discharge** | **Baseline test**‡ | **Δ** **Baseline to discharge**§ | **Δ Discharge to 12 wk. after**  | **Δ** **Baseline to 12 wk. after discharge** | **P**|| | **P**¶ | **P\*\*** | **P**†† |
| **30-s CST std. (no. of stands**‡‡**)**MedianQ1, Q3 | 0 0, 6 | 0 0, 2 | 1 0, 6 | 3 0, 10 | 1 0, 8 | 0 0, 1 | 2 0, 6 | 2 0, 7 | 0.334 | 0.885 | 0.795 | 0.322 |
| n, analysis | 30 | 60 | 29 | 30 | 30 | 61 | 29 | 30 |  |  |  |  |
| **30-s CST mod. (no. of stands**‡‡**)**MedianQ1, Q3 | 6 4, 8 | 1 0, 2 | 0 -1, 4 | 1 0, 4 | 5 3, 7 | 1 -1, 3 | 2 0, 4 | 3 0, 5 | 0.309 | 0.338 | 0.339 | 0.445 |
| n, analysis | 14 | 34 | 13 | 14 | 30 | 35 | 15 | 14 |  |  |  |  |
| **30-s CST-progression** |  |  |  |  |  |  |  |  |  |  |  |  |
|  Improvement N % | - | 43 71.7 | 18 62.1 | 24 77.4 | - | 34 55.7 | 24 82.8 | 22 73.3 | - | 0.069 | 0.078 | 0.711 |
|  No change N % | - | 7 11.7 | 4 13.8 | 6 19.4 | - | 10 16.4 | 0 0.0 | 2 6.7 | - | 0.454 | 0.112 | 0.255 |
|  Decline N % | - | 10 16.7 | 7 24.1 | 1 3.2 | - | 17 27.9 | 5 17.2 | 6 20.0 | - | 0.139 | 0.517 | 0.053 |
| n, analysis |  | 60 | 29 | 31 |  | 61 | 29 | 30 |  |  |  |  |
| **Stand, no use of arms**N% | 22 36.1 | 1 1.7 | 7 21.9 | 9 28.1 | 24 39.3 | 1 1.6 | 8 27.6 | 6 20.0 | 0.312 | 1.000 | 0.605 | 0.455 |
| n, analysis | 32 | 60 | 32 | 32 | 30 | 61 | 29 | 30 |  |  |  |  |
| **Body composition**§§ |  |  |  |  |  |  |  |  |  |  |  |  |
|  **Total LBM** (kg) Median Q1, Q3 | 45.9 36.9, 51.1 | -0.4 -2.1, 1.0 | 0.2-0.6, 2.2 | 0.4-3.2, 1.9 | 43.640.4, 55.7 | -0.2-1.4, 0.7 | 0.6-0.8, 4.3 | 1.7-0.5, 5.4 | 0.324 | 0.614 | 0.548 | 0.052 |
|  **LBM arms** (kg) Median Q1, Q3 | 4.73.5, 5.7 | -0.1-0.3, 0.0 | 0.1-0.1, 0.3 | -0.1-0.5, 0.2 | 4.74.0. 5.8 | -0.1-0.2, 0.1 | 0.0-0.3, 0.4 | -0.1-0.2, 0.3 | 0.394 | 0.106 | 0.435 | 0.493 |
| **Supplementary Table 3 continued…** |
|  | **Protein group**† | **Placebo group**† |  |  |  |  |
|  | **Baseline test**‡ | **Δ** **Baseline to discharge**§ | **Δ Discharge to 12 wk. after**  | **Δ** **Baseline to 12 wk. after discharge** | **Baseline test**‡ | **Δ** **Baseline to discharge**§ | **Δ Discharge to 12 wk. after**  | **Δ** **Baseline to 12 wk. after discharge** | **P**|| | **P**¶ | **P\*\*** | **P**†† |
|  **LBM legs** (kg) Median Q1, Q3 | 12.38.8, 15.2 | 0.3 -0.3, 0.8 | 0.3 -0.3, 1.1 | 0.6-.1, 1.2 | 12.811.1, 16.9 | 0.1-0.2, 0.8 | 0.70.3, 1.8 | 1.00.4, 1.4 | 0.141 | 0.735 | 0.179 | 0.271 |
|  **LBM torso** (kg) Median Q1, Q3 | 19.016.2, 22.5 | -0.2-0.8, 0.2 | 0.4 -0.5, 1.0 | 0.0-1.2, 0.4 | 20.017.7, 22.9 | -0.2-0.6, 0.3 | 0.3-0.6, 1.0 | 0.1-0.4, 0.7 | 0.317 | 0.344 | 0.754 | 0.302 |
|  **Total Fat Mass** (kg) Median Q1, Q3 | 22.616.8, 27.6 | 0.2-0.8, 1.3 | 0.1 -1.5, 1.5 | 1.0 0.1, 2.3 | 23.517.1, 30.1 | 0.2-0.6, 1.1 | 1.4-1.4, 3.5 | 0.6-2.1, 3.1 | 0.260 | 0.615 | 0.199 | 0.767 |
| n, analysis | 31 | 58 | 30 | 31 | 25 | 53 | 25 | 25 |  |  |  |  |
| **BMI (kg/m2)**MedianQ1, Q3 | 25.3 22.6, 27.6 | -0.03 -0.4, 0.3 | 0.4 -0.1, 0.9 | 0.2 -0.6, 1.0 | 25.423.1, 30.4 | 0.04 -0.4, 0.3 | 1.0 0.5, 1.4 | 0.9 0.3, 1.5 | 0.353 | 0.835 | **0.032** | **0.050** |
| n, analysis | 32 | 59 | 30 | 32 | 30 | 60 | 27 | 28 |  |  |  |  |
| **Handgrip strength (kg)**MedianQ1, Q3 | 19.711.5, 24.4 | 0.3 -1.8, 1.9 | 0.6 -1.4, 3.7 | 0.5 -2.4, 2.6 | 18.011.8, 25.5 | -0.3 -2.3, 2.1 | 1.6 -1.2, 4.0 | 0.7 -1.8, 5.5 | 0.927 | 0.563 | 0.612 | 0.394 |
| n, analysis | 32 | 61 | 31 | 32 | 28 | 61 | 27 | 28 |  |  |  |  |
| **DEMMI (0-100)**MedianQ1, Q3 | 57 48, 67 | 5 0, 12 | 6 -1, 22 | 120, 26 | 51 44, 62 | 4 -4, 10 | 5 0, 15 | 14 5, 26 | 0.228 | 0.878 | 0.969 | 0.646 |
| n, analysis | 31 | 60 | 30 | 31 | 29 | 61 | 28 | 29 |  |  |  |  |
| **4-m Gait speed (m/s)**MedianQ1, Q3 | 0.70.5, 0.9 | 0.02-0.1, 0.2 | 0.1 -0.1, 0.2 | 0.03 -0.1, 0.2 | 0.50.4, 0.7 | 0.0 -0.1, 0.2 | 0.2 -0.01, 0.2 | 0.20.1, 0.3 | 0.071 | 0.959 | 0.314 | **0.026** |
| n, analysis | 32 | 60 | 30 | 32 | 29 | 58 | 27 | 29 |  |  |  |  |
| **Barthel (0-100)**MedianQ1, Q3 | 80 76, 94 | 13 3, 27 | 0 -2, 5 | 13 2, 21 | 77 49, 86 | 19 6, 35 | 0 -1, 5 | 21 9, 39 | 0.085 | 0.143 | 0.742 | **0.033** |
| n, analysis | 31 | 57 | 31 | 31 | 28 | 59 | 29 | 28 |  |  |  |  |
| **Supplementary Table 3 continued…** |
|  | **Protein group**† | **Placebo group**† |  |  |  |  |
|  | **Baseline test**‡ | **Δ** **Baseline to discharge**§ | **Δ Discharge to 12 wk. after**  | **Δ** **Baseline to 12 wk. after discharge** | **Baseline test**‡ | **Δ** **Baseline to discharge**§ | **Δ Discharge to 12 wk. after**  | **Δ** **Baseline to 12 wk. after discharge** | **P**|| | **P**¶ | **P\*\*** | **P**†† |
| **MMSE score (0-30)**MedianQ1, Q3 | 26 23, 28 | 1 0, 2 | 0 -1, 2 | 1 0, 2 | 27 22, 28 | 1 -1, 3 | -1 -1, 1 | 2 -1, 3 | 0.904 | 0.683 | 0.532 | 0.575 |
| n, analysis | 31 | 61 | 31 | 31 | 30 | 61 | 29 | 30 |  |  |  |  |
| **QoL score (-0.55-1)**MedianQ1, Q3 | 0.719.649, .806 | 0.000 -.022, .126 | 0.000 -.076, .055 | 0.000 -.063, .164 | 0.722.693, .818 | 0.055 .000, .183 | 0.000 -.055, .126 | 0.070 -.024, .157 | 0.966 | 0.195 | 0.364 | 0.228 |
| n, analysis | 32 | 61 | 31 | 32 | 30 | 61 | 29 | 30 |  |  |  |  |
| **QoL VAS (0-100)**MedianQ1, Q3 | 50 41, 65 | 4 -7, 20 | 5 -9, 20 | 15 0, 29 | 50 44, 70 | 0 -10, 12 | 0 -10, 14 | 8 -4, 20 | 0.610 | 0.319 | 0.398 | 0.413 |
| n, analysis | 32 | 60 | 31 | 32 | 30 | 60 | 28 | 30 |  |  |  |  |
| **Abbreviations:** CST, Chair-stand-test: std, standard (arms crossed across the chest): Q1, first quartile: Q3, third quartile: mod, modified (use of help, e.g. arm rest): LBM, Lean Body Mass: BMI, Body Mass Index: DEMMI, De Morton Mobility Index: MMSE, Mini Mental State Examination: QoL, Quality of Life: VAS, Visual Analogue Scale.**\* Statistical tests:** Mann-Whitney test (median (Q1, Q3)), and Chi-square/Fisher’s exact test (counts < 5) (n (%)). †Includes only participants with high compliance (average consumption of ≥ 75 % of the total dose of intervention product).‡Includes only those with high compliance throughout the entire study. Baseline performance for the highly compliant during the period from baseline to discharge are comparable to that shown in Table 5+6. §Duration in days (median (Q1, Q3)): protein group 5 days (4, 8), n=32 & Placebo group 6 days (3, 8), n=30.||P-values for differences between groups at baseline.¶P-values for differences between groups during hospitalization.**\*\*** P-values for differences between groups during the period 12 weeks after discharge.†† P-values for differences between groups for the whole intervention period.‡‡ No differences between groups in height of chair at any time point.§§ Measured using dual-frequency Bio-impedance analysis.Δ: indicate ‘changes from’ |