Effects of a 12-week Vivifrail Exercise Program on intrinsic capacity among frail cognitively impaired community-dwelling older adults: Secondary analysis of a multicenter randomized clinical trial

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**Supplementary Table 1.** Features of exercise programs according to Vivifrail level (A, B, C or D) (for more details visit [www.vivifrail.com](http://www.vivifrail.com))

The resistance exercises started with 2 sets of ten repetitions with a 30-repetition maximum (RM) (e.g., weight that allows to do the exercise 30 times yet makes them feel they have made effort) load at week 1 and progressed to 3 sets of 12-15 repetitions at 20 RM in week 12. For the balance exercises, difficulty was increased by duration length (10s to 30s), sensory deprivation (e.g., performance with eyes closed) and increasingly difficult contexts (performance on unstable surfaces such as foam rolls or adding obstacles). Subjects were encouraged to challenge their ability for postural stability during exercises while assuring safety to avoid falls. Flexibility exercises progressed in terms of repetitions (from 2 to 3) and duration (10s-20s) along the program. Finally, the aerobic component of the Vivifrail program was adapted to each functional level with durations ranging from 5-7 repetitions of 5-10s walks (week 1) to 12-15 repetitions of 60s walks at week 12 in the functional level A (SPPB 0-3); to 2 sets of 15 minutes at week 1 to 50-70 minutes at week 12 in the functional level D (SPPB 10-12)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Level A** | **Level B** | **Level C** | **Level D** |
|  | **Wk.** | **Sets /reps** | **Load** | **Exercises** | **Exercises** | **Exercises** | **Exercises** |
| **Strength** | 1-2 | 2/10 | 30RM | Sitting arm curl, ball squeeze or towel roll-up (handgrip), shoulder extension with elastic band, sitting calf-raise, sitting knee extension, sitting hip abduction | Sitting arm curl, ball squeeze or towel roll-up (handgrip), shoulder extension with elastic band, calf-raise, sitting knee extension, hip abduction, knee flexion, assisted chair sit to stand. | Sitting arm curl, ball squeeze or towel roll-up (handgrip), shoulder extension with elastic band, standing calf-raise, sitting knee extension, hip abduction, knee flexion, chair sit to stand. | Sitting arm curl, ball squeeze or towel roll-up (handgrip), shoulder extension with elastic band, standing calf-raise, hip abduction, knee flexion, chair sit to stand, stairs climb |
| 3-4 | 2/12-15 |
| 5-6 | 3/12 |
| 7-8 | 2/10 | 20RM |
| 9-10 | 2/12-15 |
| 11-12 | 3/12-15 |
| **Balance** | **Wk.** | **Sets /duration** | Assisted tandem walk, assisted toes to heel roll | Assisted tandem walk, one-leg standing assisted toes to heel roll, tiptoe walking, heel walking | Tandem walk, one-leg standing, toes to heel roll, tiptoe walking, heel walking, walking overcoming obstacles, multi-direction walking | Tandem walk, one-leg standing toes to heel roll, tiptoe walking, heel walking, walking overcoming obstacles, multi-direction walking, walking with external distractors (balloons) |
| 1-2 | 1/10’’ |
| 3-4 | 1/15’’ |
| 5-6 | 1/30’’ |
| 7-8 | 1/30’’ |
| 9-10 | 1/30’’ |
| 11-12 | 1/30’’ |
| **Flexibility and mobility** | **Wk.** | **Sets /duration** | Arms stretching, back shoulder stretching, cervical region stretching, dorsal-plantar flexion, sitting back muscular chain stretching | Arms stretching, back shoulder stretching, cervical region stretching, dorsal-plantar flexion, sitting back muscular chain stretching | Arms stretching, back shoulder stretching, cervical region stretching, dorsal-plantar flexion, sitting back muscular chain stretching | Arms stretching, back shoulder stretching, cervical region stretching, dorsal-plantar flexion, sitting back muscular chain stretching |
| 1-2 | 2/3/10’’ |
| 3-4 |
| 5-6 |
| 7-8 | 3-3/10’’ |
| 9-10 |
| 11-12 |
| **Cardiovascular** | **Wk.** | **Sets /duration** | Walk at usual pace | Walk at usual pace | Walk at usual pace | Walk at usual pace |
| 1-2 | 5-7/5-10’’ |
| 3-4 | 5-7/10-15’’ |
| 5-6 | 5-7/10-15’’ |
| 7-8 | 5-10/15-30’’ |
| 9-10 | 5-10/30-45’’ |
| 11-12 | 12-15/45-60 |

Abbreviations: Wk: week; Reps= repetitions; RM: repetition-maximum

**Supplementary Table 2. Characteristics of included participants according to randomization groups at baseline and at the 12-week visit**

|  |  |  |
| --- | --- | --- |
|  | Baseline Values | At 3-month visit |
| **Characterstics** | Whole SampleTotal (n=188) | Control Group(n=100) | Vivifrail Group(n=88) | Whole SampleTotal (n=188) | Control Group(n=100) | Vivifrail Group(n=88) |
| **Weight, kg** | 66.66 ± 10.98 | 66.49 ± 11.41 | 66.86 ± 10.54 | 66.09 ± 11.07 | 66.58 ± 11.36 | 65.34 ± 10.68 |
| **IMC, kg.m-2, b** | 27.04 ± 3.97 | 27.02 ± 4.31 | 27.06 ± 3.57 | 26.87 ± 4.05 | 27.06 ± 4.18 | 26. 57 ± 3.87 |
| **Barthel Index (0-100)** | 91.43 ± 9.77 | 91.79 ± 10.23 | 91.13 ± 9.27 | 92.58 ± 10.51 | 92.78 ± 10.80 | 92.28 ± 10.15 |
| **GDS Yesavage score (0-15)** | 3.62 ± 2.92 | 3.36 ± 2.91 | 3.92 ± 2.92 | 3.74 ± 3.29 | 4.01 ± 3.58 | 3.32 ± 2.79 |
| **Gait speed, m/s** | 0.63 ±0.19 | 0.64 ± 0.19 | 0.61 ± 0.18 | 0.65 ± 0.24 | 0.66 ± 0.23 | 0.63 ± 0.24 |
| **5-STS, s** | 19.18 ± 13.39 | 18.38 ± 13.18 | 20.12 ± 13.64 | 17.87 ±13.07 | 18.55 ± 14.01 | 16.79 ±11.50 |
| **SPPB score (0-12)b** | 7.31 ± 2.59 | 7.73 ± 2.47 | 6.85 ± 2.66 | 7.72 ± 2.76 | 7.73 ± 2.82 | 7.69 ± 2.70 |
| **Handgrip Strength, kg** | 19.37 ± 7.23 | 19.21 ± 7.70 | 19.56 ± 6.69 | 20.38 ± 6.92 | 19.44 ± 6.98 | 21.83 ± 6.64 |
| **MoCA score (0-30)** | 15.55 ± 5.20 | 15.37 ± 5.24 | 15.81 ± 14.30 | 16.24 ± 6.17 | 15.19 ± 6.35 | 18.07 ± 5.51 |
| **IC Composite Score** | 0.06 ± 0.53 | 0.08 ± 0.55 | 0.04 ± 0.48 | 0.04 ± 0.46 | 0.04 ± 0.50 | 0.04 ± 0.38 |

Abbreviations.

1. Body mass index calculated as weight in kilograms divided by height in meters squared.
2. P < .05 based on Student T-test test or Pearson χ2 test (between Vivifrail/Control groups)

**Supplementary Table 3. CONSORT Checklist**

CONSORT 2010 checklist of information to include when reporting a randomised trial\*

|  |  |  |  |
| --- | --- | --- | --- |
| Section/Topic | Item No | Checklist item | Reported on page No |
| Title and abstract |
|  | 1a | Identification as a randomised trial in the title | Title page |
| 1b | Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) | Page 1 |
| Introduction |
| Background and objectives | 2a | Scientific background and explanation of rationale | Pages 3-4 |
| 2b | Specific objectives or hypotheses | Page 4 |
| Methods |
| Trial design | 3a | Description of trial design (such as parallel, factorial) including allocation ratio | Page 5 |
| 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | - |
| Participants | 4a | Eligibility criteria for participants | Page 6 |
| 4b | Settings and locations where the data were collected | Page 6 |
| Interventions | 5 | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | Page 6 and 7 |
| Outcomes | 6a | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | Page 7 and 8 |
| 6b | Any changes to trial outcomes after the trial commenced, with reasons | - |
| Sample size | 7a | How sample size was determined | Page 9 |
| 7b | When applicable, explanation of any interim analyses and stopping guidelines | - |
| Randomisation: |  |  |  |
|  Sequence generation | 8a | Method used to generate the random allocation sequence | Page 6 |
| 8b | Type of randomisation; details of any restriction (such as blocking and block size) | Page 6 |
|  Allocation concealment mechanism | 9 | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned | Page 6 |
|  Implementation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | Page 6 |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how | Page 6 |
| 11b | If relevant, description of the similarity of interventions | - |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes | Page 8 |
| 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses | Page 9 |
| Results |
| Participant flow (a diagram is strongly recommended) | 13a | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome | Page 9 |
| 13b | For each group, losses and exclusions after randomisation, together with reasons | Page 9 |
| Recruitment | 14a | Dates defining the periods of recruitment and follow-up | Page 5 |
| 14b | Why the trial ended or was stopped | - |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group | Page 16 |
| Numbers analysed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | Page 16 |
| Outcomes and estimation | 17a | For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | Pages 9 and 17 |
| 17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended | - |
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | Pages 10 and 11 |
| Harms | 19 | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | - |
| Discussion |
| Limitations | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | Pages 14 and 15 |
| Generalisability | 21 | Generalisability (external validity, applicability) of the trial findings | Page 15 |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | Pages 13-14 |
| Other information |  |
| Registration | 23 | Registration number and name of trial registry | Page 5 |
| Protocol | 24 | Where the full trial protocol can be accessed, if available | Page 5 |
| Funding | 25 | Sources of funding and other support (such as supply of drugs), role of funders | Title Page |

**Supplementary Table 4. Mixed-effects linear models analyses for 3-month evolution from baseline in IC domains and the IC Composite Score according to randomization groups (Males).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Intrinsic Capacity Domain** | **Time-point** | **Vivifrail Group****N=88**β (95% CI)a | **Control group****N=100**β (95% CI) | **Between-group differences**β (95% CI) | **p-value** |
| IC Locomotion domain z-score | 3-months | 0.40 (0.17, 0.64) | -0.13 (-0.29, 0.02) | 0.54 (0.30, 0.82) | **<0.001** |
| IC Cognitiondomain z-score | 3-months | 0.45 (0.01, 0.90) | -0.05 (-0.30, 0.20) | 0.50 (0.01, 0.99) | **0.046** |
| IC Vitalitydomain z-score | 3-months | 0.12 (-0.05, 0.35) | -0.03 (-0.09, 0.03) | 0.15 (-0.09, 0.39) | 0.45 |
| IC Psychologydomain z-score | 3-months | -0.24 (-0.66, 0.18) | -0.21 (-0.42, 0.00) | -0.03 (-0.48, 0.42) | 0.06 |
| **IC Composite Score** | **3-months** | **0.43 (0.16, 0.70)** | **-0.17 (-0.30, -0.04)** | **0.60 (0.30, 0.89)** | **<0.001** |

Significant associations in bold. Models were adjusted by age, sex, educational level and baseline IC level. Abbreviations: β (95%CI)= β-coefficients and 95% confidence interval; IC=Intrinsic Capacity

**Supplementary Table 5. Mixed-effects linear models analyses for 3-month evolution from baseline in IC domains and the IC Composite Score according to randomization groups (Females).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Intrinsic Capacity Domain** | **Time-point** | **Vivifrail Group****N=88**β (95% CI)a | **Control group****N=100**β (95% CI) | **Between-group differences**β (95% CI) | **p-value** |
| IC Locomotion domain z-score | 3-months | 0.15 (-0.26, 0.47) | -0.05 (-0.28, 0.17) | 0.21 (-0.18, 0.60) | 0.58 |
| IC Cognitiondomain z-score | 3-months | 0.24 (-0.43, 0.91) | -0.05 (-0.48, 0.38) | 0.29 (-0.51. 1.08) | 0.77 |
| IC Vitalitydomain z-score | 3-months | 0.36 (-0.05, 0.78) | -0.01 (-0.15, 0.13) | 0.38 (-0.06, 0.81) | 0.45 |
| IC Psychologydomain z-score | 3-months | 0.31 (-0.40, 1.02) | -0.44 (0-0.87, -0.01) | 0.75 (-0.02, 1.53) | 0.11 |
| **IC Composite Score** | **3-months** | **0.04 (-0.35, 0.42)** | **-0.28 (-0.55, 0.01)** | **0.31 (-0.13, 0.76)** | **0.20** |

Significant associations in bold. Models were adjusted by age, sex, educational level and baseline IC level. Abbreviations: β (95%CI)= β-coefficients and 95% confidence interval; IC=Intrinsic Capacity