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Older persons with signs of frailty in a home-based physical exercise intervention – baseline characteristics of an RCT

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Abstract

Background: Increasing the level of physical activity among persons with signs of frailty improves physical functioning. There is a lack of long-term supervised physical exercise intervention studies including a validated definition of frailty.

Aims: To present baseline characteristics of persons with signs of frailty participating in a randomized long-term home-based physical exercise trial (HIPFRA), and to study associations between the severity of frailty, functional independence and health-related quality-of-life (HRQoL).

Methods: Three hundred persons, ≥ 65 years old and with signs of frailty, (assessed by Fried´s phenotype criteria) were recruited from South Karelia, Finland and randomized to a 12-month physiotherapist-supervised home-based physical exercise programme (n=150), and usual care (n=150). Assessments at the participants' homes at baseline, and after three, six and 12 months included the Short Physical Performance Battery (SPPB), the Functional Independence Measure (FIM), HRQoL (15D) and the Mini-Mental State Examination (MMSE).

Results: Eligibility was screened among 520 persons; 300 met the inclusion criteria and were randomized. One person withdrew consent after randomization. A majority (75%) were women, 182 were pre-frail and 117 frail. The mean age was 82.5 (SD 6.3) y, SPPB 6.2 (2.6), FIM 108.8 (10.6) and MMSE 24.4 (3.1) points, with no significant differences between the study groups. Inverse associations between the severity of frailty vs. FIM scores and HRQoL ($p<0.001$ for both) were found.

Conclusions: Our participants showed marked physical frailty without major disabilities. The severity of frailty seems to be associated with impaired functional independence and HRQoL.

Trial registration: ClinicalTrials.gov NCT02305433

Key words: frailty, exercise, disability, health-related quality-of-life, community-dwelling older people

1 Introduction

Frailty syndrome is characterized by diminished strength, endurance and reduced physiological functions, and can lead to vulnerability, disability, falls, long-term care and mortality [1, 2]. Frailty occurs more commonly in women. Its prevalence increases with age, varying between 4-59% depending on the definition and the population studied [3]. A consensus of opinion on how to screen, define and assess frailty has not been reached [4]. Various methods can be used to screen and identify persons with signs of frailty, for example Fried´s frailty phenotype [5], the Frailty Index [6] and the FRAIL questionnaire [7]. Fried´s frailty phenotype criteria [5] are often used to assess physical frailty, and there are five items: 1) unintentional weight loss, 2) low physical activity, 3) exhaustion, 4) weak grip strength and 5) slow walking speed. If a person meets one or two criteria, he/she is considered as pre-frail, and if a person meets three or more criteria he/she is considered as frail [5].

One characteristic of frailty is a low physical activity level [5]. Increasing physical activity among frail persons improves physical functioning (e.g. strength, mobility, balance, and flexibility) [8]. Short-term multicomponent exercise programmes have improved physical functioning [9], frailty status [9], and quality-of-life [10] in frail persons. A longer duration of training (more than five months) seems to have greater effects on health than shorter ones in frail older adults [11]. Older adults feel that it is safer to exercise when training is supervised [12], and under supervision the intensity can be higher [13]. Further benefits of physical training in frail persons may result from individualized programmes, which seem to have greater effects on mobility and physical functioning than group exercises [14]. However, there is a scarcity of exercise trials that have involved the use of validated definitions of frailty. In particular, there is a lack of long-term supervised physical exercise trials. Along with our study, the ongoing SPRINTT trial [15] is targeted on physically frail and sarcopenic older people, with the aim of filling this gap

Our randomized controlled study HIPFRA is a real-life long-term supervised physical exercise study, targeted on home-dwelling, well-defined pre-frail and frail older adults and designed to assess the effects of physical exercise training on the duration of residing at home, and on functioning and health-related quality-of-life. The aim of this report is to describe baseline characteristics and associations between the severity of frailty vs. functional independence and quality-of-life in a-randomized controlled trial involving long-term supervised home-based physical exercise.

2 Methods

2.1 Design

Our frailty group is part of the HIPFRA study [16], which is a randomized controlled trial carried out to investigate the effects of 12-month supervised physical exercise intervention on the days lived at home in a 24-month period (the primary outcome). Secondary outcomes are physical functioning, health-related quality-of-life (HRQoL), severity of frailty, and use of social and health-care services. The intervention group

participates in supervised home-based physical exercise (60-minute sessions twice a week) for 12 months, and the usual care group continues to live as usual. The hypothesis is that physical exercise intervention postpones institutionalisation and increases the time living at home by six months. The trial received approval from the Coordinating Ethics Committee of Helsinki University Hospital, Finland and is registered at ClinicalTrials.gov (NCT02305433). Participation was voluntary and persons interested received comprehensive oral and written information about the study-For a more detailed description see Soukkio et al. 2018 [16].

2.2 Participants and randomization

Participants were recruited from the South Karelia Social and Health Care District (population 131,000), Finland, starting in December 2014. They were informed about the study by way of flyers and advertisements in local newspapers, and by health care personnel. Inclusion criteria were age ≥65 years, home-dwelling (with or without home care services), able to walk independently inside with or without a mobility aid, ≥17 points in the Mini-Mental State Examination (MMSE) [17] and ability to communicate in Finnish. To be eligible the persons interested in participating needed to score at least one point in the FRAIL questionnaire [7], and fulfil at least one of the five frailty phenotype criteria [5] (Table 1).

Exclusion criteria were residing permanently in institutional care, and severe or advanced diseases, that prevented participation in physical exercise, such as severe neurological or cardiovascular disease with severely impaired physical capacities (NYHA class III or IV), severe or acute mental problems, alcohol or drug abuse, severe problems with hearing or eyesight or terminal illnesses.

The participants were first screened with by using the FRAIL questionnaire [7]. This questionnaire contains five items fatigue (How often during the past four weeks did you feel tired?), resistance (By yourself and not using aids do you have difficulty walking up 10 steps without resting?), ambulation (By yourself and not using aids, do you have any difficulty walking 300 meters?), physician-diagnosed illnesses (a list of 11 illnesses), and loss of weight (more than 5% from the previous year's weight). If the person scored one or more points, he/she continued to the next phase of recruitment.

The study nurse checked the person's eligibility to take part in the study, and verified frailty status and severity by using Fried´s frailty phenotype criteria (with slight modifications) [5] (Table 1). Eligible persons signed an informed consent document and the baseline assessments were performed at the participant's home. After baseline assessments, the participants were randomized to two groups: physiotherapist-supervised home-based physical exercise training (n=150), and usual care (n=150). Randomization was performed by using a computer generated random allocation sequence with varying block sizes.

2.3 Assessments

A more detailed description of the assessments can be found elsewhere [16]. The primary outcome measure, time residing at home (over a period of 24 months) was assessed from the South Karelia Social and Health

Care District's patient records and registers. In-patient care, hospital days, and institutionalised care (nursing home, sheltered housing) are considered as days not lived at home.

Secondary outcome measures are assessments performed at the participant's home at baseline, and after three, six and 12 months by the study physiotherapist or the study nurse, both trained to perform them. Each assessment visit takes about 1.5 hours~~;~~ and consists of a structured interview, questionnaires and measurements.

Physical functioning was assessed by using the Short Physical Performance Battery (SPPB) [18], the Functional Independence Measure (FIM) [19], and Lawton's instrumental activities of daily living (IADL) [20], and grip strength was measured with a Saehan dynamometer (model Sh5001, South Korea). Cognition was assessed by using the MMSE [17], depressive symptoms with the Geriatric Depression Scale (GDS-15) [21], and nutritional status by using the Mini Nutritional Assessment (MNA) [22]. IADL, FIM, GDS-15 and MNA data were assessed by interviewing the participant. To assess HRQoL the participant answered the 15D questionnaire [23]. Weight (Omron HN289 equipment, Japan) and height (KaWe Person-Check equipment, Germany) were measured, and body mass index (BMI) was calculated. Regularly used medications and diseases diagnosed by a physician were asked about. Information was completed from electronic medical records, and the Charlson comorbidity index (CCI) [24] was calculated.

Demographic factors such as age, marital status, education and former occupation, form of living, and use of home and home health-care services were inquired about in the baseline interview. Perceived health, mobility ability and physical fitness were asked about using questions from the Finnish Elderly Health survey [25]. Lifestyle habits were investigated: physical activity as weekly frequency of activity sessions lasting for more than 30 minutes, and smoking habits as the daily amounts of cigarettes and other products. Perceived pain was assessed by inquiring "Are you experiencing any pain at the moment or during the day?". The number of falls was investigated by asking "Have you fallen during the previous three months and if you did, did you have any associated injuries?".

2.4 Statistical analyses

Statistical comparisons between the randomization groups were made by using t-test and the $\chi 2$ test, as appropriate. Statistical significances for the unadjusted hypothesis of linearity across categories of frailty severity of the study participants were evaluated by using analysis of variance (ANOVA) with an appropriate contrast (orthogonal polynomial). The bootstrap method was used when the theoretical distribution of the test statistics was unknown or in cases of violation of the assumptions (e.g. non-normality). The normality of the variables was tested by using the Shapiro-Wilk W-test. The Stata 15.0, StataCorp LP (College Station, TX, USA) statistical package and IBM SPSS statistics 25.0 were used for the analyses. In the analyses two frailty categories (scores 4 and 5) were combined to achieve an appropriate amount of persons. The level of statistical significance was set at 0.05 in all analyses. For statistical power calculation see Soukkio et al. (2018) [16].

3 Results

3.1 Recruitment and baseline characteristics

Five-hundred and twenty persons were screened by using the FRAIL questionnaire. Of these 43% were screened by the health care personnel and 57% by the study personnel. Of the screened persons, 224 women and 76 men met all the inclusion criteria and were willing to participate (Fig. 1). One person withdrew their informed consent after randomization and denied use of the data, decreasing the number of participants in the usual care group to 149. The mean age was 82.5 years, (range 65 to 98). According to the frailty criteria 182 participants were pre-frail (one or two criteria of the five fulfilled), and 117 were frail (3-5 criteria fulfilled) at baseline. Nine participants fulfilled all five frailty criteria (Table 1). The mean SPPB score was 6.2 (SD 2.6), and the mean FIM total score was 108.8 (10.6). Of the participants, 239 (80 %) used a rollator walker or stick. One hundred and seventy-four (58%) lived alone, and 25% received home care or home health care services organized through the hospital district. The groups were similar in their baseline characteristics (Table 2).

Fig. 1 Flowchart of the study

Table 1. Frequency of frailty criteria and their distribution in the physical exercise and usual care groups. The p-values refer to a difference between the randomization groups.

Frailty phenotype criteria [a]	**Participants meeting the criteria, n, (%)**			
	All (n= 299)	**Physical exercise** (n=150)	**Usual care** (n=149)	**p-value**
Unintentional weight loss				
more than 5 % (vs. weight 12 months ago)	53 (18)	26 (17)	27 (18)	0.86
Low physical activity [b]				
Under 30 minutes per week	160 (54)	77 (51)	83 (66)	0.45
Exhaustion				
Answering "moderate amount" or "most of the time" to one or both questions: How often did you feel that…	186 (62)	90 (60)	96 (64)	0.43
a) everything you did was an effort?	141 (47)	64 (43)	77(52)	
b) you could not get going?	122 (41)	59 (39)	63 (42)	
Weakness				
Weak grip strength under cut-off value [c]	179 (60)	94 (63)	85 (57)	0.32
Slowness				
Gait speed [d] < 0.46 m/s	81 (27)	48 (32)	33 (22)	0.051

[a] Slightly modified, [b] Minutes per week were used instead of kcal per week. Our question was "How often did you exercise during the previous three months?", [c] Cut-off values (stratified by BMI and gender): for women with BMI ≤ 26.0 kg/m^2, cut-off ≤ 17 kg; BMI 26.1-29.0 kg/m^2, cut-off ≤ 18 kg; BMI >29.0 kg/m^2, cut-off ≤ 21 kg. For men with BMI ≤ 24.0 kg/m^2, cut-off ≤ 29 kg; BMI 24.1-28.0 kg/m^2, cut-off ≤ 30 kg; BMI >28.0 kg/m^2 cut-off ≤ 32 kg ,[d] Normal gait speed, walking aid allowed, cut-offs, at 4 m >8.7 s and at 2.44 m > 5.2 s.

Table 2. Baseline characteristics of all participants and in the randomized groups (physical exercise and usual care). Frequencies (%) or means (SD) are shown. Values of p refer to differences between the randomization groups.

Characteristics	All (n=299)	Physical exercise (n=150)	Usual care (n=149)	p-value
Women, n (%)	224 (75)	114 (76)	110 (74)	0.67
Age, mean (SD)	82.5 (6.3)	82.2 (6.3)	82.7 (6.3)	0.44
BMI [a] (kg/m^2), mean (SD)	28.5 (5.9)	28.4 (5.5)	28.6 (6.1)	0.78
Marital status, n (%)				0.19
Married/in a relationship	118 (39)	56 (37)	62 (42)	
Single/divorced	46 (15)	19 (13)	27 (18)	
Widowed	135 (45)	75 (50)	60 (40)	
Education <9 years, n (%)	195 (63)	99 (66)	90 (60)	0.32
MMSE [b], mean (SD)	24.4 (3.1)	24.2 (3.1)	24.6 (3.2)	0.39
Severity of frailty [c]				0.94
Pre-frail, 1-2 of the 5 criteria, n (%)	182 (61)	91 (61)	91 (61)	
Frail, 3-5 of the 5 criteria, n (%)	117 (39)	59 (39)	58 (39)	
Physician-diagnosed diseases or disorders, n (%)				
Coronary heart disease	128 (43)	57 (38)	71 (48)	0.09
Stroke or TIA [d]	70 (23)	37 (25)	33 (22)	0.61
Hypertension	220 (74)	110 (73)	110 (74)	0.92
Musculoskeletal diseases [e]	253 (85)	129 (86)	124 (83)	0.51
Respiratory diseases (COPD [f], asthma)	36 (12)	16 (11)	20 (13)	0.46
Depressive symptoms	50 (17)	25 (17)	25 (17)	0.98
Alzheimer's disease or other dementias	41 (14)	19 (13)	22 (15)	0.60
CCI [g], mean (SD)	2.0 (1.7)	2.0 (1.7)	2.0 (1.7)	0.84
Number of regular medications, mean (SD)	6.8 (3.1)	6.7 (3.2)	7.0 (3.1)	0.43
Walking aids, n (%)	239 (80)	122 (81)	117 (79)	0.54
Walking sessions (> 30 minutes) weekly, n (%)				0.11
4-7 times	37 (12)	15 (10)	22 (15)	
1-3 times	79 (26)	47 (31)	32 (21)	
<1 time	183 (61)	88 (59)	95 (64)	
Grip strength [h] (kg), mean (SD)				
Women	16.5 (5.5)	16.3 (5.7)	16.7 (5.3)	0.53
Men	27.7 (7.6)	27.3 (7.6)	28.2 (7.7)	0.61
SPPB [i], mean (SD)	6.2 (2.6)	6.1 (2.7)	6.3 (2.5)	0.49
FIM [j], mean (SD)				
Total	108.8 (10.6)	108.8 (10.3)	108.8 (10.9)	0.97
Motor	78.0 (7.8)	78.0 (7.6)	78.0 (8.0)	0.92
Cognition	30.9 (4.0)	30.9 (4.0)	31.0 (3.9)	0.85
HRQoL 15D [k], mean (SD)	0.712 (0.091)	0.719 (0.084)	0.705 (0.097)	0.19
GDS-15 [l], mean (SD)	4.8 (2.7)	4.7 (2.5)	4.9 (2.8)	0.64
MNA [m], mean (SD)	23.1 (3.2)	23.3 (3.1)	22.7 (3.4)	0.15
Falls during the previous 3 months, n (%)				0.89
none	192 (64)	98 (65)	94 (64)	
1-2	80 (27)	40 (27)	40 (27)	
≥ 3	26 (9)	12 (8)	14 (9)	
Perceived pain [n], n (%)	217 (73)	103 (69)	114 (77)	0.07

[a] BMI, Body Mass Index; [b] MMSE, Mini-Mental State Examination [17]; [c] Severity of frailty measured with modified Fried´s phenotype criteria[5]; [d] TIA, Transient Ischaemic Attack; [e] Musculoskeletal diseases, at least one of the following: arthritis, osteoporosis, rheumatoid arthritis, low back pain; [f] COPD, Chronic Obstructive Lung Disease; [g] CCI, Charlson Comorbidity Index [24]; [h] Mean of the best values (of three tries) from both hands; [i] SPPB, Short Physical Performance Battery [18]; [j] FIM, Functional Independence Measure [19]; [k] Health-related quality-of-life questionnaire (15D) [23]; [l] GDS-15, Geriatric Depression Scale- 15 [21]; [m] MNA, Mini Nutritional Assessment [22]; [n] Answering "yes" to the question, "Are you experiencing any pain at the moment or during the day?".

3.2. Severity of frailty, and functional independence

The severity of frailty was inversely and linearly associated with FIM scores (Fig. 2). With an increase in the number of frailty criteria met, FIM scores decreased. In the pre-frail participants the mean FIM score was 113 (SD 8) and in the frail persons it was 103 (11) (p for linearity <0.001). The same pattern was seen in both FIM subcomponents; in the motor component the mean score in the pre-frail persons was 81 (SD 6) and in the frail persons 74 (9) (p for linearity < 0.001), and in the cognition component the mean scores were 32 (4) and 30 (4) (p < 0.001), respectively.

Fig. 2 FIM (Functional Independence Measure) scores (total, cognition and motor) by categories of frailty severity (frailty scores 1, 2, 3, and 4-5) at baseline. Mean (95 % CI). The total number of participants was 299, of whom 91 persons were in category 1, 91 in category 2, 82 in category 3, and 35 in category 4-5. Values of p are for linearity across frailty categories

3.3. Severity of frailty, and health-related quality-of-life

An inverse association between severity of frailty and HRQoL was also seen (Fig. 3). Those who were frail (scores 3-5) had lower scores in the 15D questionnaire, indicating worse quality-of-life compared with persons with pre-frailty (p for linearity <0.001).

Fig. 3 Health-related quality-of-life (15D) scores by categories of frailty severity (frailty scores 1, 2, 3, and 4-5) at baseline. Mean (95% CI). The total number of participants was 299, of whom 91 persons were in category 1, 91 in category 2, 82 in category 3, and 35 in category 4-5. Values of p are for linearity across frailty categories

4 Discussion

We recruited 300 persons with signs of frailty and randomized them to physical exercise and usual care groups. We were able to recruit both pre-frail and frail persons. The participants' physical functioning at baseline according to SPPB scores was impaired while most of them did not have major problems in functional independence. The severity of frailty was linearly associated with both physical functioning and HRQoL.

Slightly modified phenotype criteria were used to detect older persons with signs of frailty. During the recruitment process, we were able to recruit a high number of physically frail older adults from the area of South Karelia. Recruitment had two main sources; advertisements and health-care personnel. The personnel's information about eligible candidates was important for us to find those more severely physically frail persons. On the other hand, persons who contacted us directly were usually in better condition.

According to the frailty characteristics, our participants were markedly physically frail. A majority of participants were pre-frail (61%) with low SPPB scores, which gives us an opportunity to observe changes in frailty status during the intervention year. In our trial the two most prevalent frailty criteria were weakness

(60%) and exhaustion (62%). Findings from two large population-based studies [26] revealed that weakness was the first frailty criterion, occurring as early as nine years prior to the onset of frailty, while low physical activity and slowness occurred six years prior to onset. The last frailty criterion occurring at or before the onset of frailty was weight loss [26]. Among our participants, the occurrence of weight loss was only 18%, being in line with the results of other studies [5, 27].

The participants' mean age was high, they suffered from multiple diseases and often reported polypharmacy, most of them lived alone and a very high proportion (80%) used mobility devices. Even though the majority of our participants were pre-frail, their mean SPPB scores were relatively low compared with those reported in the LIFE [28], and SPRINTT [29] studies, and by Tarazona-Santabalbina et al.[9], reflecting our participants' prevailing physical frailty, which can be considered as a strength of this study. On the other hand, the SPRINTT [29] and LIFE [30] studies did not involve participants needing mobility devices, and frailty phenotype as an inclusion criterion was not used.

The mean FIM score of 109 among our participants indicates fairly independent functioning compared for example, with that in Finnish Alzheimer exercise trial, where the mean FIM score was 87 [31]. A declining FIM score reflects more dependence on help from others in everyday chores. In our study an inverse association between the severity of frailty and functional independence was observed. A negative association has been found between Edmonton Frailty Scale (EFS) and FIM scores in patients at discharge from a short-term geriatric ward [32]. To our knowledge the association between frailty and FIM scores has not been studied before in community-living older adults. It seems that the severity of frailty also shows an inverse association ~~also~~ with HRQoL and our findings are in line with those in previous studies [33, 34].

A strength of our study is that it is a rigorously performed randomized controlled trial, in real life. The participants are truly physically frail or pre-frail thus indicating neither ceiling nor floor effects on our outcomes. Another strength is that we used validated measurements and questionnaires. The research physiotherapist and the nurse were trained to perform the assessments and are monitored. Assessments and the intervention are performed in the participants' homes, so they need no transportation. As a weakness, the study assessors cannot be blinded since they participated in scheduling the trial although they do not administer the exercise intervention. Furthermore, our primary aim of increasing the duration of home-living by six months is relatively large. However, this frail population is at high risk of use of hospital and other institutional care. The risk of contamination of the groups is relatively low since the participants' baseline physical activity is very low and the supply of physiotherapy for this patient group is limited in public health care.

5 Conclusions

Recruitment of the participants was successful. At baseline the characteristics of the two groups were similar. The participants were physically frail or pre-frail according to modified Fried´s phenotype criteria. The occurrence of the five frailty phenotype criteria were in line with the findings of other studies. An increase in the number of frailty phenotype criteria seems to be associated with a decline in functional independence and in health-related quality-of-life.

Ethics approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. A written informed consent was obtained from all individual participants included in the study.

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Conflicts of interest: The authors declare that they have no conflicts of interest.

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