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Strength but not power training increases soluble alpha klotho levels in pre-frail older adults

Michaela Rippl [a,*], Martin Bidlingmaier [b], Linda Deissler [a], Sebastian Martini [a], Katharina Mueller [a], Sabine Schluessel [a], Ralf Schmidmaier [a,b], Júnia R.O.L. Schweizer [b], Olivia Tausendfreund [a], Laura Welscher [a], Michael Drey [a]

[a] LMU Munich Hospital, Department of Medicine IV, Geriatrics, Ziemssenstr. 5, 80336, Munich, Germany
[b] LMU Munich Hospital, Department of Medicine IV, Endocrinology, Ziemssenstr. 5, 80336, Munich, Germany

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ABSTRACT

Background: Loss of physical function is a growing health concern in aging populations. Resistance training, including strength training (ST) and power training (PT), is the main therapeutic approach, yet evidence regarding the most effective modality remains inconsistent. Soluble alpha klotho (sαKL) is a protein increasingly recognized for its role in muscle function and may serve as a biomarker of training responsiveness due to its association with aging, muscle integrity, and exercise-induced adaptions. Therefore, we aimed to investigate whether ST and PT differentially influence sαKL levels in older adults.

Methods: 69 prefrail, community-dwelling older adults (65–94 years) were randomly assigned to 12 weeks of ST, PT, or a control group (ClinicalTrials.gov: NCT00783159). In a post hoc analysis serum sαKL levels and physical performance measures before and after the intervention were analyzed.

Results: 23 participants were allocated to ST, 24 to PT and 22 to the control group. The participants had a mean age of 77 years, 70 % were female. There were no baseline differences between groups. Both ST and PT led to significant improvements in the Short Physical Performance Battery (SPPB) but only ST increased sαKL levels.

Conclusion: Twelve weeks of ST, but not PT, significantly increased circulating sαKL levels in pre-frail older adults. Given the beneficial health effects of increased sαKL, these findings suggest that ST may offer additional biological advantages relevant to healthy aging. sαKL may serve as a promising biomarker for training-induced adaptions, but prospective trials are needed to confirm long-term effects and further clarify underlying mechanisms.

1. Introduction

The progressive loss of physical function with age represents a major public health concern in aging societies (Reid and Fielding, 2012). Preventing or delaying this decline is therefore a key public health goal. Aging is a natural life stage marked by physical, psychological, and social changes. Regular physical activity is one of the most effective non-pharmacological strategies to support healthy aging, as it enhances quality of life, functional capacity, and independence (Sanchís-Soler et al., 2025). Living alone may reduce motivation and functional ability, underscoring the value of strength training and community-based exercise programs (Parra-Rizo et al., 2022). Because pre-frail individuals are at high risk of functional decline but can potentially return to a robust state, they represent an important target group for training interventions. (Kojima et al., 2019) The main therapeutic approach for improving physical decline is resistance training, which includes different types such as strength training (ST) and power training (PT) (Steib et al., 2010). Strength training aims to increase maximal muscle strength through slow, equally long controlled concentric and eccentric contractions (Siddique et al., 2022). Power training (PT) in contrast accelerates the concentric phase while maintain a controlled eccentric phase, targeting muscle power – the amount of work performed per unit of time (Balachandran et al., 2022; Drey et al., 2012). Recent evidence suggests that both approaches improve muscle function in older adults, yet they may target different physiological deficits. While ST enhances maximal force production, PT has been shown to enhance rapid force

* Corresponding author.
E-mail address: michaela.rippl@med.uni-muenchen.de (M. Rippl).

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generation, which is crucial for tasks such as preventing falls or rising from a chair (Colón-Emeric et al., 2024). Because age-related functional decline is often accompanied by a greater decline in muscle power than strength, PT may provide particular benefits for maintaining functional independence (da Rosa Orssatto et al., 2019; El Hadouchi et al., 2022). Nevertheless, findings in the literature remain inconsistent, with some trials reporting superior functional outcomes with PT but also reported a lack of high quality and high heterogeneity among the studies (Balachandran et al., 2022; da Rosa Orssatto et al., 2019). Additionally, no study has incorporated molecular biomarkers that could objectively quantify training-induced adaptations.

From a clinical perspective, given this limited and inconsistent evidence, it remains difficult to determine which type of training—PT or ST—is truly superior. Perhaps, rather than relying solely on clinical impressions, it would be more informative if an objective measurement would be available.

Recent evidence points to soluble alpha-klotho (sαKL), a transmembrane protein primarily expressed in the kidney but also present in muscle tissue, as a potential mediator of exercise-induced benefits. (Lim et al., 2015; Amaro-Gahete et al., 2018). Because sαKL overexpression is linked to increased lifespan and various health advantages, it is considered an "anti-aging" protein (Crasto et al., 2012). Conversely, low circulating levels of sαKL have been associated with frailty, sarcopenia, and reduced strength, whereas exercise appears to modulate its expression (Veronesi et al., 2021; Amaro-Gahete et al., 2019a; Corrêa et al., 2022).

Given its role in muscle integrity sαKL represents a promising biomarker for evaluating training responses. Determining whether different training modalities influence sαKL to varying degrees may help to clarify mechanisms behind functional improvements and support more personalized exercise prescriptions.

Despite the ongoing debate about the optimal training modality, the specific effects of ST and PT on molecular mediators such as sαKL in older adults remain unclear. Understanding these effects could provide mechanistic insights into how exercise promotes healthy aging and help establish sαKL as a potential biomarker of training responsiveness. To our knowledge, no study has yet investigated whether ST and PT differentially influence circulating sαKL levels in pre-frail older adults. This gap is particularly important, as identifying modality-specific biomarker responses may clarify inconsistent clinical findings and enhance evidence-based recommendations for early-stage interventions.

2. Material and methods

2.1. Participants and study design

Participants were drawn from a randomized, controlled training study in prefrail, community-dwelling older adults (Drey et al., 2011). Participants aged 65–94 years were recruited via newspaper advertisements, insurance mailings, and local geriatric centers. Of 663 screened individuals, 298 were eligible for frailty assessment, 69 were finally randomized into three groups (ST, PT, control). Exclusion criteria were: GDS (geriatric depression scale) >5, dementia characterized as MMSE (mini mental status examination) < 25, BMI (body mass index) > 35 kg/m2, intake of immunosuppressive drugs, history of kidney stones, sarcoidosis, plasmacytoma, COPD, inflammatory bowel disease, angina pectoris, history of cancer, and current attendance of muscle training. Pre-frailty was defined according to Fried's criteria (≥1 and ≤ 2 components of the frailty phenotype) (Fried et al., 2001). Participants meeting one or two of the criteria were classified as pre-frail and consecutively included in the intervention. Of 298 subjects who attended the (pre-)frailty screening 182 did not meet the (pre-)frailty criteria and 47 rejected participation, leading to the inclusion of 69 participants into the study. Stratified by sex the remaining subjects were randomized into the strength training ($n = 23$), power training ($n = 24$), and control group ($n = 22$). A detailed flow chart showing the recruitment and randomization process can be found in Drey et al., 2012 (Drey et al., 2012). Randomization was performed by an independent study collaborator who was not involved in other parts of the study, using computer-generated blocks of 12–15 participants. The participants received sealed envelopes containing the group assignment by the blinded assessor. A detailed description of the applied measurements has been published before (Drey et al., 2012).

2.2. Intervention

The intervention lasted 12 weeks and included two supervised sessions per week (60 min each).

Each training session began with a 5-min warm up consisting of walking exercises, followed by 20 min of balance training performed on the floor, on mats, and on wobble boards, combined with ball-catching exercises.

In both groups, resistance training was carried out using the "Bodyspider" machine (KOOPERA, Germany), a device that generates resistance through elastic bands. Exercises included chest press, standing hip extension/flexion, standing hip adduction/abduction, tip-toe raises, and chair rise. All exercises except tip-toe raises and chair rises, were performed on the "Bodyspider" machine, whereas the latter two were executed without additional weight but with maximum repetitions. The PT group was instructed to perform explosive resistance training, moving as fast as possible during the concentric phase of each repetition and slowly during the eccentric phase (approximately 2–3 s). In contrast the ST group performed the same exercises, but both concentric and eccentric contractions were executed at the same average velocity (approximately 2–3 s). Both groups completed two sets of each exercise, with a two-minute rest period between sets. In accordance with the guidelines of McDermott and Mernitz (McDermott and Mernitz, 2006), training intensity was adjusted every two weeks by increasing tensile strength, progressing from Borg's Rate of Perceived Exertion (RPE) of 10–11 in the initial weeks to 16 in the final week (Borg, 1998). Qualified instructors supervised all training sessions, ensuring correct movement velocity and providing encouragement. Attendance was recorded, and adherence was defined as participation in ≥80 % of sessions. All participants were instructed to maintain their usual activity levels throughout the study period. Participants in the control group did not perform training but were invited to attend two lectures on physical activity and healthy nutrition during the study. To enhance compliance, control group participants were offered the opportunity take part in a combined ST and PT program after completion of the intervention. The detailed training protocol has already been described elsewhere (Drey et al., 2012).

2.3. Frailty assessment

Frailty was assessed according to the criteria developed by Fried et al. (Fried et al., 2001), including unintentional weight loss of more than 10 lb. in the past year, self-reported exhaustion based on the Center for Epidemiologic Studies-Depression Scale (CES-D scale), weakness defined as reduced handgrip strength according to the original criteria, slow walking speed based on the 15-ft gait test at normal pace, and low physical activity based on the Minnesota Leisure Time Physical Activity Questionnaire (MLTPAQ) (Fried et al., 2001; Taylor et al., 1978; Radloff, 1977).

2.4. Baseline measures

At baseline, functional status was evaluated using the Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) questionnaires (Katz, 1983; Collin et al., 1988). Responses were documented on the corresponding forms and used to calculate the respective scores. In addition, trained study personnel administered the Mini-Mental State Examination (MMSE) to assess cognitive function

(Folstein et al., 1975).

2.5. Outcome measures

Physical performance was measured objectively using the short physical performance battery (SPPB), sit-to-stand transfer test (STS-Power), and handgrip strength (as part of the Frailty screening). The SPPB is a well-established tool comprising balance-tests, timed 4-m walk and the chair rise test (Guralnik et al., 1994). It ranges from 0 (low performance) to 12 points (high performance). The SPPB has been described in detail before (Guralnik et al., 1994). Also, muscular power of the lower limb was assessed using the sit-to-stand transfer test described by Lindemann et al. (Lindemann et al., 2003). Participants sat on the front edge of a chair (seat height: 49 cm) with their arms crossed over their chest, eyes directed forward, and both feet placed on a force plate (Zebris Medical, Germany). They were instructed to stand up as quickly as possible and then remain still until data collection was complete. Each participant completed the test three times, with a one-minute break between attempts. Throughout all trials, the examiner provided verbal encouragement to promote explosive movement. Sit-to-Stand (STS) power was calculated from force plate data obtained during the rising phase, reflecting how much power participants generated to stand up, taking into account their body weight and movement speed. The best performance across the three trials was used for analysis. The method has been described in more detail before (Drey et al., 2012). Handgrip strength was measured according to Fried et al. (Fried et al., 2001).

In addition to objective performance assessments, a self-reported measure of physical function—the German version of the Short Form of the Late Life Function and Disability Instrument (SF-LLFDI), specifically its function component—was used (Denkinger et al., 2009). This questionnaire was administered both at the start and upon completion of the training intervention. It evaluates functional capabilities in three domains: advanced lower extremity, basic lower extremity, and upper extremity function. The tool is recognized for its reliability and validity in older populations (Haley et al., 2002). Scores were recorded as individual values on a scale from 0 to 100.

2.6. Laboratory analyses

Soluble alpha klotho (sαKL) was measured using the Sandwich ELISA (Enzyme-Linked Immunosorbent Assay) by Immuno Biological Laboratories, Hamburg (RRID:AB_2750859) before and after the training intervention. A detailed description of the assay is published elsewhere (Yamazaki et al., 2010; Schweizer et al., 2025). Mean within-assay CVs for the low and high QC pools pipetted at the beginning and the end of each plate were 1.8 % and 1.5 %, respectively. Overall, between-assay-CVs were 6.1 % and 4.0 %, respectively (Schweizer et al., 2025). Serum creatinine-levels were measured before the intervention using kinetic color test based on Jaffé-method. The laboratory personnel were blinded to the allocated study-groups.

2.7. Statistical analysis

All statistical analyses were performed using the IBM SPSS software (Version 29.0.0.0; IBM Corp., Armonk, NY, USA). Metric variables are presented as mean and standard deviation (SD), categorical data are shown as number (n) and percent (%). Intergroup differences were analyzed using one-way analysis of variance (ANOVA) for parametric and Chi-square-test for non-parametric variables.

Missing data occurred only in few cases, were clearly marked, and were excluded from the respective analyses. Normality checks were not performed, as the sample size was considered sufficiently large for the central limit theorem to apply. The level of statistical significance was set at $p \leq 0.05$.

After adjustment for potential confounders the associations of the investigated types of training (ST and PT) with sαKL levels, SPPB, balance, CRT, gait time, handgrip strength, SFLLFDI and STS Power were analyzed using linear regression analysis and presented as regression coefficients with 95 %-confidence intervals. Included covariables were added in Models 1–3 as follows:

- Model 1: type of training
- Model 2: + age, sex
- Model 3: + creatinine

No correction for multiple comparisons was applied, as the analyses were primarily exploratory and based on a limited number of predefined hypotheses. Effect sizes and 95 % confidence intervals were reported to support interpretation of the results.

2.8. Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of the local University (20–0823). It was also registered at clinicaltrials.gov as NCT00783159. All participants gave written informed consent.

3. Results

3.1. Baseline characteristics

The baseline characteristics are displayed in Table 1. The total study group consisted of 69 participants of which 23 were allocated to the strength training group (ST), 24 to the power training group (PT) and 22 to the control group (CT). Overall age was 77 years with no significant differences between the training groups. Approximately 70 % of the study group were female. No significant differences between the groups were found for all variables.

Table 1
Baseline characteristics.

Characteristic	Strength (ST)	Power (PT)	Control (CT)	p-value (ANOVA)
	n = 23	n = 24	n = 22	
Age, years	77 ± 6	78 ± 6	76 ± 8	0.603
Female, n (%)	16 (70)	16 (67)	16 (73)	0.905[#]
BMI, kg/m^2	29.5 ± 4.4	28.0 ± 4,0	28.4 ± 4.2	0.450
ADL, points	99 ± 2	98 ± 4	99 ± 3	0.619
IADL, points	7 ± 1	7 ± 1	7 ± 1	0.741
MMSE, points	29 ± 1	29 ± 2	28 ± 1	0.404
sαKL, pg/ml	806 ± 200[a b]	904 ± 260[c]	821 ± 233	0.351
Creatinine mg/dl	0.9 ± 0.3	0.9 ± 0.2	0.9 ± 0.3	0.888
Handgrip strength, kg	25 ± 6	24 ± 6	24 ± 8	0.794
Gait time, s	4.6 ± 1.7	3.9 ± 1.0	3.8 ± 0.8	0.072
CRT, s	15 ± 7	12 ± 3[a]	12 ± 4	0.071
Balance, points	3 ± 1	2 ± 1	3 ± 1	0.051
SPPB, points	9 ± 2	9 ± 2[b]	10 ± 2	0.080
SFLLFDI, points	118 ± 16	121 ± 16	117 ± 20	0.662
STS power, Watt	467 ± 170	501 ± 146[a]	459 ± 173	0.658

ADL: activities of daily living, IADL: instrumental activities of daily living, MMSE: mini mental status examination, aLM: appendicular lean mass, CRT: chair rise test, SPPB: short physical performance battery, SFLLFDI: Short Form of the Late Life Function and Disability Instrument, STS: sit-to-stand, sαKL: soluble alpha klotho

[a] : $n = 22$

[b] : $n = 23$.

[c] : $n = 20$

[#] : Chi-2-Test.

3.2. Delta soluble alpha klotho levels

Fig. 1 displays the change in absolute sαKL levels from pre- to post-intervention, expressed as delta sαKL levels. Only strength training led to a significant increase in sαKL levels, whereas in both the power training and control groups sαKL levels tended to decrease without reaching statistical significance. Table 2 summarizes the descriptive statistics of sαKL levels.

3.3. Effects of strength and power training

Tables 3 and 4 present the linear regression analyses comparing the strength training (ST) group to the control (CT) group (Table 3), and the power training (PT) group to the control group (Table 4). Strength training (Table 3) showed significant associations with changes in sαKL levels, chair rise test (CRT) and short physical performance battery (SPPB) throughout all regression models. Power training (Table 4) only showed a significant association with changes in SPPB throughout all regression models. In both groups, the type of training was not significantly associated with changes in any of the other variables.

Table 2
Descriptive statistics of sαKL levels.

	Strength (ST)	Power (PT)	Control (CT)
sαKL, pg/ml pre	806 ± 200; 791	904 ± 260; 869	821 ± 233; 775
sαKL, pg/ml post	834 ± 206; 816	885 ± 274; 786	806 ± 249; 742
sαKL, pg/ml Delta	27 ± 60; 19	−19 ± 88; −10	−16 ± 68; −16

Values are presented as: mean ± standard deviation; median

Table 3
Regression analyses examining the associations between training mode and changes in sαKL levels and physical performance in the strength training (ST) versus control group.

Strength training vs. control			
Dependent variable	Model 1	Model 2	Model 3
Delta sαKL	**43.09 (4.24–81.94)***	**45.04 (5.92–84.16)***	**44.14 (3.77–84.51)***
Delta SPPB	**1.55 (0.38–2.71)***	**1.52 (0.32–2.72)***	**1.59 (0.37–2.83)***
Delta Balance	0.59 (−0.29–1.48)	0.57 (−0.34–1.48)	0.58 (−0.36–1.52)
Delta CRT	**−3.75 (−6.51-(−0.99))***	**−3.67 (−6.47-(−0.869))***	**−4.21 (−6.99-(−1.43))***
Delta Gait time	−0.46 (−0.95–0.03)	−0,48 (−0.97–0.01)	**−0.58 (−1.06-(−0.10))***
Delta Handgrip strength	0.08 (−2.34–2.49)	0.07 (−2.42–2.56)	0.42 (−2.07–2.90)
Delta SFLLFDI	−2.60 (−7.28–2.07)	−2.78 (−7.46–1.91)	−2.82 (−7.63–1.99)
Delta STS Power	31.67 (−27.77–91.09)	25.77 (−31.11–82.65)	32.50 (−25.12–90.13)

Model 1: type of training, model 2: + age, sex, model 3: + creatinine.
CRT: Chair rise test, SPPB: short physical performance battery, SFLLFDI: Short Form of the Late Life Function and Disability, Instrument, STS: sit-to-stand, sαKL: soluble alpha klotho.
* : $p \leq 0.05$.

4. Discussion

Our study demonstrated a significant increase in sαKL levels in community-dwelling pre-frail older adults following 12 weeks of strength but not power training.

This finding is noteworthy, as training per se has been shown to increase sαKL concentrations; however, the impact of different types of resistance training—especially in older adults—remains unclear and points towards a potential association between sαKL stimulation and the type of resistance training (Corrêa et al., 2022). Supporting our hypothesis, Neves et al. found an improvement in the sclerostin/FGF23/klothos axis following 6 months of dynamic but not isometric resistance training (Neves et al., 2021). Comparable to our cohort dynamic resistance training consisted of 12 exercises using elastic bands, dumbbells or body weight with an equal duration (2 s.) of the concentric and excentric phase (Neves et al., 2021). Interestingly, despite the fact that their study cohort consisted of clearly younger (average age approximately 56 years) maintenance hemodialysis patients, we observed similar results in our older pre-frail but kidney-healthy participants (Neves et al., 2021). Notably, our finding remained statistically significant after adjustment for kidney function, which is important, given the well-established influence of renal function and sαKL levels (Rotondi et al., 2015). Conversely, Estébanez et al. could not find alterations in the klotho protein content in peripheral blood mononuclear cells following resistance training in elderly subjects (on average 73 of age) for 8 weeks

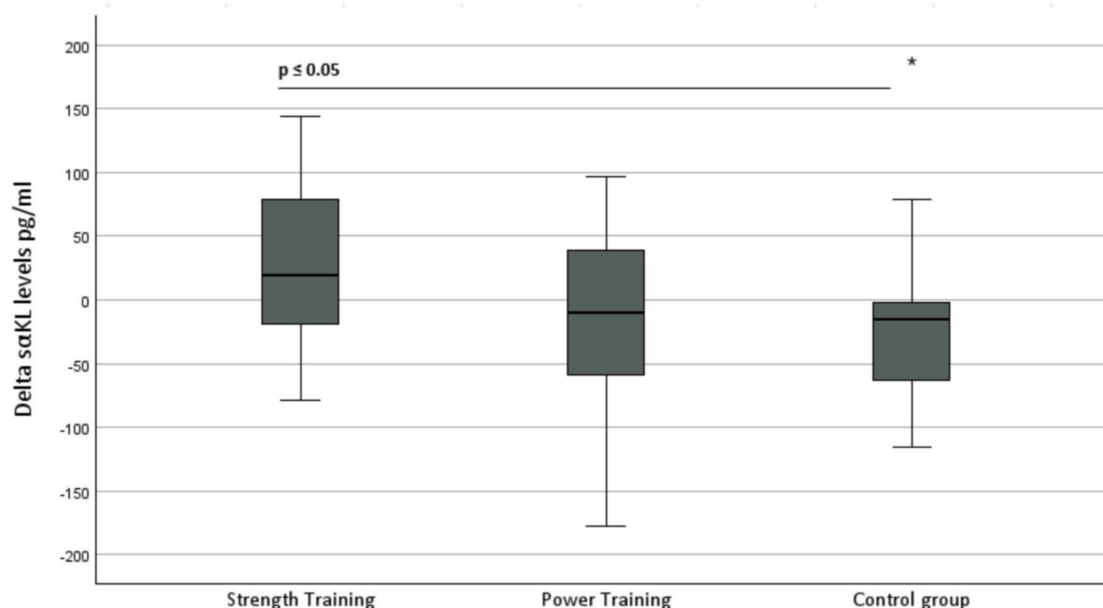

Fig. 1. showing the delta sαKL levels in the strength training, power training and control group (* marks an outlier).

Table 4
Regression analyses examining the associations between training mode and changes in sαKL levels and physical performance in the power training (PT) versus control group.

Power training v. control			
Dependent variable	Model 1	Model 2	Model 3
Delta sαKL	−3.71 (−52.43–45.00)	−2.47 (−51.85–46.91)	−4.49 (−54.72–45.73)
Delta SPPB	**1.45 (0.39–2.52)***	**1.46 (0.36–2.56)***	**1.48 (0.36–2.60)***
Delta Balance	**1.07 (0.17–1.98)***	**1.05 (0.12–1.97)***	**1.05 (0.09–1.99)***
Delta CRT	−0.68 (−1.62–0.25)	−0.71 (−1.66–0.24)	−0.68 (−1.66–0.29)
Delta Gait time	−0.08 (−0.43–0.27)	−0.20 (−0.46–0.22)	−0.13 (−0.47–0.22)
Delta Handgrip strength	0.31 (−1.98–2.61)	0.32 (−2.04–2.68)	0.44 (−1.96–2.84)
Delta SFLLFDI	−2.87 (−8.23–2.49)	−3.08 (−8.57–2.39)	−3.51 (−9.01–1.98)
Delta STS Power	−14.43 (−73.33–44.48)	−22.15 (−74.33–30.03)	−20.52 (−73.81–32.77)

Model 1: type of training, model 2: + age, sex, model 3: + creatinine.
CRT: Chair rise test, SPPB: short physical performance battery, SFLLFDI: Short Form of the Late Life Function and Disability Instrument, STS: sit-to-stand, sαKL: soluble alpha klotho.
* : $p \leq 0.05$.

(Estébanez et al., 2022). Nevertheless, unlike our study cohort the participants examined by Estèbanez et al. were healthy older adults, and the study assessed klotho protein content instead of sαKL, rendering the results not directly comparable (Estébanez et al., 2022). Middelbeek et al. also found an increase in sαKL levels following two weeks of moderate intensity exercise compared to sprint training in healthy middle-aged men (Middelbeek et al., 2021). Our findings thus provide additional support for the hypothesis that ST may provide a sufficiently long muscle fiber tension to stimulate PPAR-γ, thereby increasing sαKL secretion, whereas PT may not and extend this evidence to a geriatric patient population.

Current exercise recommendations for older adults increasingly emphasize power training, as declines in muscle power occur earlier and more rapidly than declines in muscle strength and are strongly linked to mobility limitations and fall risk (Reid and Fielding, 2012; El Hadouchi et al., 2022). Consequently, PT is often promoted as the preferred training modality to counteract age-related functional decline (El Hadouchi et al., 2022). Against this backdrop, our finding that ST—but not PT—enhanced sαKL levels is particularly noteworthy. It suggests that while PT may offer functional advantages, ST may provide additional biological benefits related to sαKL regulation, potentially adding a complementary dimension to exercise prescription in older adults.

When exploring possible explanations for this, one important difference between strength and power training is the duration of the tension phase (Balachandran et al., 2022). It is relatively long and constant in strength training but very short in power training. sαKL excretion is, among others, known to be mediated by the Peroxisome-activated receptor-γ (PPAR-γ) (Zhang et al., 2008). Activation of PPAR-γ on the other hand is promoted by exercise training, which may explain the link between increasing sαKL levels after physical training (Thomas et al., 2012; Amaro-Gahete et al., 2019b). Therefore, only ST may provide a sufficiently long muscle fiber tension to stimulate PPAR-γ, thereby increasing sαKL secretion, whereas PT may not. However, the exact pathways leading to an increase in sαKL levels only after ST but not after PT remain unclear.

Regarding physical performance, despite the differentiating increases in sαKL, both training groups (ST and PT) showed improvements as measured only by the SPPB, but not in other outcomes. Interestingly, the groups improved in different subcomponents of the SPPB —the ST group in the chair rise test (CRT) and the PT group in the balance component (Zech et al., 2012). The improvement of the ST group in the CRT is particularly noteworthy, as lower-limb muscle power, which is required for this task, is crucial for maintaining mobility and preventing limitations in activities of daily living, as well as reducing the risk of falls in older adults (Colón-Emeric et al., 2024; Braun et al., 2022). Therefore, this finding has practical relevance, as ST not only enhances muscle power but, through the stimulation of sαKL as described above, may also increase a biomarker linked to longevity and muscle health and could guide exercise prescription in pre-frail older adults.

Since our study cohort consisted of pre-frail participants, we wondered about the association between sαKL levels and (pre-)frailty status. In the review by Veronesi et al., findings regarding the association between sαKL levels and frailty were inconsistent (Veronesi et al., 2021). While one study reported no significant relationship, Shardell et al. identified a potential cut-off value >660 pg/ml for sαKL with lower odds of becoming pre-frail or frail (Shardell et al., 2019; Polat et al., 2020). Beyond this review, data from the NHANES 2007–2016 cohort further support the link between sαKL and frailty, revealing an L-shaped relationship with a turning point at 785.7 pg/ml. (Jiang et al., 2023). Also, a recent bidirectional Mendelian randomization study further supports a causal inverse relationship between sαKL and frailty index but did not define a fixed cut-off value (Zhu et al., 2025). In this context, it is also important to note the established relationship between muscle power and frailty progression. Burbank et al. demonstrated in a large cohort that reduced muscle power was associated with higher odds of pre-frailty and frailty and influenced the likelihood of improving or worsening frailty status over a four-year period (Burbank et al., 2023). Although our study primarily examined the relationship between resistance training and sαKL levels rather than frailty outcomes, these findings highlight the clinical relevance of identifying training modalities that can beneficially influence trajectories of (pre-)frailty.

However, given these cut-offs for sαKL and frailty one might realize that mean sαKL levels in our study population were higher than the given cut-off ranges even though we only included participants classified as pre-frail and not frail. With a mean age of 74 years, the study cohort by Shardell et al. was comparable to ours, and also frailty criteria according to Fried et al. were applied, thus not accounting for the discrepancy (Shardell et al., 2019). However, in the study by Jiang et al. and Zhu et al., frailty was assessed using a frailty index and given the mean age of 62.76 years in the study population by Jiang et al. the cohort was younger than ours (Jiang et al., 2023; Zhu et al., 2025). Baseline sαKL levels in our pre-frail cohort were also higher than reference values for 77-year-olds, likely reflecting preserved kidney function and cohort variability (Schweizer et al., 2025; Rotondi et al., 2015). However, this finding is noteworthy, as sαKL levels are generally described to decline with age but population selection, age, and preserved kidney function seem to counteract this trend (Espuch-Oliver et al., 2022). Additionally, obesity has been associated with lower sαKL levels; however, in our study cohort, individuals with severe obesity (BMI $\geq$ 35 kg/m^2) were excluded, which may also have contributed to the overall higher sαKL concentrations (Shu et al., 2025). This consideration is noteworthy given that in the study by Shardell et al. for example, over 60 % of participants were categorized as overweight or obese (Shardell et al., 2019). However, because in this study all individuals with a BMI $\geq$ 25 kg/m^2 were classified as obese, it remains unclear how many participants were truly obese ($\geq$ 35 kg/m^2) which also limits comparability with our cohort (Shardell et al., 2019).

Taken together, within the ongoing debate on the most effective type of training in older adults, our study may provide a new perspective. Considering the recognized role of elevated sαKL levels in promoting health and longevity, the increase observed after ST in our cohort offers new insight into the potential of strength training to positively influence sαKL regulation. Moreover, our findings suggest that sαKL could serve as a potential biomarker for training-induced health benefits. Nevertheless, since long-term studies are lacking, the potential long-term effects of elevated sαKL levels following ST remain to be determined in future

research.

5. Strengths and limitations

A strength of our study is the precise selection of study participants including a careful assessment of pre-frailty according to standardized criteria. Also, the study was designed as a randomized controlled trial. Since there is an ongoing search for easily accessible biomarkers to evaluate training adaptations, our study may contribute by identifying sαKL as a promising candidate. One limitation is the retrospective analysis of sαKL levels. Also, the study had a relatively small sample size and a short follow-up duration. Additionally, we acknowledge that the specific resistance profile of elastic bands may have influenced the exact mechanical stimulus delivered, which should be considered when interpreting the results. Therefore, long-term follow-ups, larger sample sizes, the inclusion of training modalities that more closely reflect the established definitions of power training, and a profound exploration of the underlying molecular mechanisms are needed.

6. Conclusion

This study demonstrates that 12 weeks of strength training, but not power training, significantly increases circulating sαKL levels in pre-frail older adults. These findings suggest that ST may be the more effective exercise modality for promoting musculoskeletal health and potentially healthy aging, with sαKL serving as a promising biomarker of training-induced benefits. Future long-term studies are needed to confirm these effects and explore underlying mechanisms.

CRediT authorship contribution statement

Michaela Rippl: Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis. **Martin Bidlingmaier:** Resources, Investigation. **Linda Deissler:** Writing – review & editing. **Sebastian Martini:** Writing – review & editing. **Katharina Mueller:** Writing – review & editing. **Sabine Schluessel:** Writing – review & editing. **Ralf Schmidmaier:** Writing – review & editing, Conceptualization. **Júnia R.O.L. Schweizer:** Resources, Investigation. **Olivia Tausendfreund:** Writing – review & editing. **Laura Welscher:** Writing – review & editing, Formal analysis. **Michael Drey:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used OpenAI. (2025) (ChatGPT (GPT-5)) in order to improve the readability and language of the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

Declaration of competing interest

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Data availability

The data that has been used is confidential.

References

Amaro-Gahete, F.J., De-la, O.A., Jurado-Fasoli, L., Espuch-Oliver, A., de Haro, T., Gutiérrez, Á., et al., 2019a. Body composition and S-klotho plasma levels in middle-aged adults: a cross-sectional study. Rejuvenation Res. 22 (6), 478–483.

Amaro-Gahete, F.J., De-la, O.A., Jurado-Fasoli, L., Espuch-Oliver, A., de Haro, T., Gutierrez, A., et al., 2019b. Exercise training increases the S-klotho plasma levels in sedentary middle-aged adults: a randomised controlled trial. The FIT-AGEING study. J. Sports Sci. 37 (19), 2175–2183.

Amaro-Gahete, F.J., OA, de-la, Jurado-Fasoli, L., Ruiz, J.R., Castillo, M.J., Gutiérrez, Á., 2018. Role of exercise on S-klotho protein regulation: a systematic review. Curr. Aging Sci. 11 (2), 100–107.

Balachandran, A.T., Steele, J., Angielczyk, D., Belio, M., Schoenfeld, B.J., Quiles, N., et al., 2022. Comparison of power training vs traditional strength training on physical function in older adults: a systematic review and Meta-analysis. JAMA Netw. Open 5 (5), e2211623.

Borg, G., 1998. Borg's Perceived Exertion and Pain Scales, viii. Human Kinetics, Champaign, IL, US, p. 104 viii.

Braun, T., Thiel, C., Peter, R.S., Bahns, C., Büchele, G., Rapp, K., et al., 2022. Association of clinical outcome assessments of mobility capacity and incident disability in community-dwelling older adults - a systematic review and meta-analysis. Ageing Res. Rev. 81, 101704.

Burbank, C.M., Branscum, A., Bovbjerg, M.L., Hooker, K., Smit, E., 2023. Muscle power predicts frailty status over four years: a retrospective cohort study of the National Health and aging trends study. J Frailty Sarcopenia Falls. 8 (1), 1–8.

Collin, C., Wade, D.T., Davies, S., Horne, V., 1988. The Barthel ADL index: a reliability study. Int. Disabil. Stud. 10 (2), 61–63.

Colón-Emeric, C.S., McDermott, C.L., Lee, D.S., Berry, S.D., 2024. Risk assessment and prevention of falls in older community-dwelling adults: a review. JAMA 331 (16), 1397–1406.

Corrêa, H.L., Raab, A.T.O., Araújo, T.M., Deus, L.A., Reis, A.L., Honorato, F.S., et al., 2022. A systematic review and meta-analysis demonstrating klotho as an emerging exerkine. Sci. Rep. 12 (1), 17587.

Crasto, C.L., Semba, R.D., Sun, K., Cappola, A.R., Bandinelli, S., Ferrucci, L., 2012. Relationship of low-circulating "anti-aging" klotho hormone with disability in activities of daily living among older community-dwelling adults. Rejuvenation Res. 15 (3), 295–301.

Denkinger, M.D., Igl, W., Coll-Planas, L., Bleicher, J., Nikolaus, T., Jamour, M., 2009. Evaluation of the short form of the late-life function and disability instrument in geriatric inpatients-validity, responsiveness, and sensitivity to change. J. Am. Geriatr. Soc. 57 (2), 309–314.

Drey, M., Pfeifer, K., Sieber, C.C., Bauer, J.M., 2011. The Fried frailty criteria as inclusion criteria for a randomized controlled trial: personal experience and literature review. Gerontology 57 (1), 11–18.

Drey, M., Zech, A., Freiberger, E., Bertsch, T., Uter, W., Sieber, C.C., et al., 2012. Effects of strength training versus power training on physical performance in prefrail community-dwelling older adults. Gerontology 58 (3), 197–204.

El Hadouchi, M., Kiers, H., de Vries, R., Veenhof, C., van Dieën, J., 2022. Effectiveness of power training compared to strength training in older adults: a systematic review and meta-analysis. Eur. Rev. Aging Phys. Act. 19 (1), 18.

Espuch-Oliver, A., Vázquez-Lorente, H., Jurado-Fasoli, L., de Haro-Muñoz, T., Díaz-Alberola, I., López-Velez, M.D.S., et al., 2022. References values of soluble α-klotho serum levels using an enzyme-linked immunosorbent assay in healthy adults aged 18-85 years. J. Clin. Med. 11 (9).

Estébanez, B., Visavadiya, N.P., Vargas, J.E., Rivera-Viloria, M., Khamoui, A.V., de Paz, J.A., et al., 2022. Resistance training modulates reticulum endoplasmic stress, independent of oxidative and inflammatory responses, in elderly people. Antioxidants (Basel). 11 (11).

Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12 (3), 189–198.

Fried, L.P., Tangen, C.M., Walston, J., Newman, A.B., Hirsch, C., Gottdiener, J., et al., 2001. Frailty in older adults: evidence for a phenotype. J. Gerontol. A Biol. Sci. Med. Sci. 56 (3), M146–M156.

Guralnik, J.M., Simonsick, E.M., Ferrucci, L., Glynn, R.J., Berkman, L.F., Blazer, D.G., et al., 1994. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J. Gerontol. 49 (2), M85–M94.

Haley, S.M., Jette, A.M., Coster, W.J., Kooyoomjian, J.T., Levenson, S., Heeren, T., et al., 2002. Late life function and disability instrument: II. Development and evaluation of the function component. J. Gerontol. A Biol. Sci. Med. Sci. 57 (4), M217–M222.
Jiang, Z., Wang, J., Cai, X., Wang, P., Liu, S., 2023. L-shaped association of serum α-klotho and frailty among the middle-aged and older adults: results from NHANES 2007-2016. BMC Geriatr. 23 (1), 716.
Katz, S., 1983. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. J. Am. Geriatr. Soc. 31 (12), 721–727.
Kojima, G., Taniguchi, Y., Iliffe, S., Jivraj, S., Walters, K., 2019. Transitions between frailty states among community-dwelling older people: a systematic review and meta-analysis. Ageing Res. Rev. 50, 81–88.
Lim, K., Groen, A., Molostvov, G., Lu, T., Lilley, K.S., Snead, D., et al., 2015. A-Klotho expression in human tissues. J. Clin. Endocrinol. Metab. 100 (10), E1308–E1318.
Lindemann, U., Claus, H., Stuber, M., Augat, P., Muche, R., Nikolaus, T., et al., 2003. Measuring power during the sit-to-stand transfer. Eur. J. Appl. Physiol. 89 (5), 466–470.
McDermott, A.Y., Mernitz, H., 2006. Exercise and older patients: prescribing guidelines. Am. Fam. Physician 74 (3), 437–444.
Middelbeek, R.J.W., Motiani, P., Brandt, N., Nigro, P., Zheng, J., Virtanen, K.A., et al., 2021. Exercise intensity regulates cytokine and klotho responses in men. Nutr. Diabetes 11 (1), 5.
Neves, R.V.P., Corrêa, H.L., Deus, L.A., Reis, A.L., Souza, M.K., Simões, H.G., et al., 2021. Dynamic not isometric training blunts osteo-renal disease and improves the sclerostin/FGF23/klotho axis in maintenance hemodialysis patients: a randomized clinical trial. J. Appl. Physiol. (1985). 130 (2), 508–516.
Parra-Rizo, M.A., Díaz-Toro, F., Hadrya, F., Pavón-León, P., Cigarroa, I., 2022. Association of co-Living and age on the type of sports practiced by older people. Sports (Basel). 10 (12).
Polat, Y., Yalcin, A., Yazihan, N., Bahsi, R., Mut Surmeli, D., Akdas, S., et al., 2020. The relationship between frailty and serum alpha klotho levels in geriatric patients. Arch. Gerontol. Geriatr. 91, 104225.
Radloff, L.S., 1977. The CES-D scale: a self-report depression scale for research in the general population. Appl. Psychol. Meas. 1 (3), 385–401.
Reid, K.F., Fielding, R.A., 2012. Skeletal muscle power: a critical determinant of physical functioning in older adults. Exerc. Sport Sci. Rev. 40 (1), 4–12.
da Rosa Orssatto, L.B., de la Rocha Freitas, C., Shield, A.J., Silveira Pinto, R., Trajano, G. S., 2019. Effects of resistance training concentric velocity on older adults' functional capacity: a systematic review and meta-analysis of randomised trials. Exp. Gerontol. 127, 110731.
Rotondi, S., Pasquali, M., Tartaglione, L., Muci, M.L., Mandanici, G., Leonangeli, C., et al., 2015. Soluble α -klotho serum levels in chronic kidney disease. Int. J. Endocrinol. 2015, 872193.
Sanchís-Soler, G., Sebastiá-Amat, S., Parra-Rizo, M.A., 2025. Mental health and social integration in active older adults according to the type of sport practiced. Acta Psychol. 255, 104920.
Schweizer, J., Schilbach, K., Haenelt, M., Gagliardo, A., Peters, A., Thorand, B., et al., 2025. Soluble alpha klotho-impact of biological variables and reference intervals for adults. Eur. J. Endocrinol. 192 (5), 631–640.
Shardell, M., Semba, R.D., Kalyani, R.R., Bandinelli, S., Prather, A.A., Chia, C.W., et al., 2019. Plasma klotho and frailty in older adults: findings from the InCHIANTI study. J. Gerontol. A Biol. Sci. Med. Sci. 74 (7), 1052–1057.
Shu, Y., Yang, J., Dou, L., Wu, M., 2025. Metabolically healthy across body mass index categories in relation to serum klotho levels: a population-based study. Front. Endocrinol. (Lausanne) 16, 1539983.
Siddique, U., Frazer, A.K., Avela, J., Walker, S., Ahtiainen, J.P., Howatson, G., et al., 2022. Determining the cortical, spinal and muscular adaptations to strength-training in older adults: a systematic review and meta-analysis. Ageing Res. Rev. 82, 101746.
Steib, S., Schoene, D., Pfeifer, K., 2010. Dose-response relationship of resistance training in older adults: a meta-analysis. Med. Sci. Sports Exerc. 42 (5), 902–914.
Taylor, H.L., Jacobs, D.R., Schucker, B., Knudsen, J., Leon, A.S., Debacker, G., 1978. A questionnaire for the assessment of leisure time physical activities. J. Chronic Dis. 31 (12), 741–755.
Thomas, A.W., Davies, N.A., Moir, H., Watkeys, L., Ruffino, J.S., Isa, S.A., et al., 2012. Exercise-associated generation of PPARγ ligands activates PPARγ signaling events and upregulates genes related to lipid metabolism. J. Appl. Physiol. (1985). 112 (5), 806–815.
Veronesi, F., Borsari, V., Cherubini, A., Fini, M., 2021. Association of Klotho with physical performance and frailty in middle-aged and older adults: a systematic review. Exp. Gerontol. 154, 111518.
Yamazaki, Y., Imura, A., Urakawa, I., Shimada, T., Murakami, J., Aono, Y., et al., 2010. Establishment of sandwich ELISA for soluble alpha-klotho measurement: age-dependent change of soluble alpha-klotho levels in healthy subjects. Biochem. Biophys. Res. Commun. 398 (3), 513–518.
Zech, A., Drey, M., Freiberger, E., Hentschke, C., Bauer, J.M., Sieber, C.C., et al., 2012. Residual effects of muscle strength and muscle power training and detraining on physical function in community-dwelling prefrail older adults: a randomized controlled trial. BMC Geriatr. 12, 68.
Zhang, H., Li, Y., Fan, Y., Wu, J., Zhao, B., Guan, Y., et al., 2008. Klotho is a target gene of PPAR-gamma. Kidney Int. 74 (6), 732–739.
Zhu, Y., Hong, G.J., Hu, Y., Wu, R., 2025. Relationship of α-klotho with frailty index and sarcopenia: a bidirectional Mendelian randomization study. Rejuvenation Res. 28 (3), 146–155.