Are muscle characteristics associated with the effect of exercise training on muscle strength in rheumatic diseases and sarcopenia? - an explorative study The Care for Muscle (C4M) Study

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Primary Objective: To study the association between muscle characteristics (contractile, morphological,biochemical, and histological) and the response to high- and low-load exercise training on muscle strength in patients with rheumatoid arthritis (...

Ethical review	Approved WMO
Status	Pending
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON57399

Source
ToetsingOnline

Brief title
C4M

Condition

- Joint disorders

Synonym
osteoarthritis lay term: rheumatic diseases, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: TKI- Health Holland,Haptic Link, Beusichem, The Netherlands, Soundtomics VU, Amsterdam the Netherlands

Intervention

Keyword: Exercise therapy, Resistance training, Rheumatic diseases, Sarcopenia

Outcome measures

Primary outcome

The primary study parameter is the difference in isokinetic muscle strength

pre- and post-intervention in all three patient groups. Quadricepsstrength

(isokinetic, BIODEX)

Secondary outcome

- A set of biomarkers obtained by muscle biopsy and blood that characterize

muscle quality in terms of energy management, histology (architecture), gene

expression and inflammation.

- Feasibility: therapy adherence, drop-out rate, user satisfaction, Net

Promoter score (Reichheld 2003)

- Subject characteristics (age, gender, height, weight, comorbidity (CIRS),

medication, educational level, employment, marital status, smoking and alcohol

use, duration symptoms, use of walking devices

- Anthropometrics: BMI, absolute & relative muscle mass (Bio Impedance

Analysis). Short-form mini- nutritional assessment (MNA-SF, Rubenstein 2001).

- Disease characteristics: diagnosis, radiologic severity RA/OA

- Performance: Muscle endurance (Biodex), Handgrip strength (JAMAR),Short Physical Performance Battery (SPPB), Six Minute Walking Test (6MWT), FITMAX survey, Meijer 2021), PROMIS short form-CAT pain, fatigue, physical function, social function.

- Muscle architecture (by ultrasound) Volume, CSA, muscle pennation angle, fascicle length.

Study description

Background summary

C4M hypothesizes that patients with low muscle strength may respond differently to different types of exercise intervention, dependent on the underlying aetiology, i.e. impaired protein synthesis versus metabolic dysfunction. This response is related to various clinical, blood-based, and muscle metabolic and architectural biomarkers and the clinical diagnosis, i.e., rheumatoid arthritis (RA), osteoarthritis (OA), and sarcopenia alone (SARC). Understanding the underlying biochemical muscle characteristics of each diagnosis group can help to develop more targeted training in making it more effective.

Study objective

Primary Objective: To study the association between muscle characteristics (contractile, morphological,biochemical, and histological) and the response to high- and low-load exercise training on muscle strength in patients with rheumatoid arthritis (RA), osteoarthritis (OA), and sarcopenia(SARC)."
Secondary objectives: To investigate the effectiveness of high- and low-load exercise on muscle endurance andclinical outcomes in patients with rheumatoid arthritis (RA), osteoarthritis (OA), and sarcopenia (SARC) and, focusing on muscular contractile, morphological, biochemical,histological characteristics, and their interaction with the three diseases."
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Study design

two-arm parallel-group exploratory trial including a total of 69 patients

Intervention

Exercise intervention 2 times a week for 8 weeks on location and once a week at home

Study burden and risks

The participant burden consists of 2 parts:
1) Measurements at baseline and follow-up. The patients are asked to go to Amsterdam UMC and/or Reade once for a biopsy and blood collection, 3D ultra sound m.quadriceps, muscle strength test m. quadriceps and a short questionnaire is administered with questions regarding physical and social functioning and perceived fatigue. Duration: in total about 150 minutes

2) The intervention/training itself. This is performed in the context of regular care, i.e. patients with low muscle strength (dynapenia according to the EWSOP criteria) who are eligible for exercise therapy. Unlike regular care, the form of the exercise therapy given is determined in advance, with the total load remaining roughly the same. Patients participating in the study will be required to come to Reade twice a week for eight weeks to complete the exercise program.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

For all patients:
Willingness and motivation to exercise. Low muscle strength defined as hand grip strength (HGS) <27 kg and <16 kg for males and females respectively. If HGS is not possible due to interfering pain or joint- deformity, the chair stand test is used instead, with low muscle strength defined as not able to rise from the chair without arms or a time >15 sec (Cruz Jentoft 2019).

- Gait speed of >0.8m/s to exclude patients who are too disabled to participate in the study (Cruz Jentoft 2019).

Osteoarthritis patients
- Ages between 50 and 70
- Patients with either knee and/or hip osteoarthritis according to clinical American College of Rheumatology criteria (Altman 1986).
- Kellgren and Lawrence (K&L) grading score of 2-4 for hip and/or knee OA.
- C-reactive Protein (CRP) levels <10mg/L within 3 months prior to enrolment

Rheumatoid arthritis patients
- Ages between 50 and 70
- Diagnosed with RA according to EULAR/ ACR criteria (Aletaha 2010).
- Disease activity score (DAS28) 2.8<5.6, as defined by the EULAR criteria (Aletaha 2010), either de novo or despite Disease-Modifying Antirheumatic Drug (DMARD) therapy.
- Stable disease three months prior to the start of the exercise intervention.
- Stable rheumatic medications three months prior to the start of the exercise intervention.
- Stopped the usage of corticosteroids 3 months prior to the start of the

exercise intervention.
- Disease duration >1 year and <15 years

Sarcopenia patients
- Ages between 50 and 80.
- Sarcopenia without joint involvement (no OA, RA), according to the EWGSOPII criteria (Cruz Jentoft 2019) of low muscle strength defined as hand grip strength (HGS) <27 kg and <16 kg for males and females respectively (dynapenia). This group will therefore involve primarily involve participants with probable sarcopenia (dynapenia) but may also encompass participants with confirmed sarcopenia (appendicular muscle Lean Mass (ALM)/height2 <7.0 kg/m2 for males and <5.5 kg/m2 for females) as this is no selection criterion. Severe sarcopenia will be excluded (gait speed < 0,8 m/s).
- Exclude patients with Joint complaints (RA, OA, or other joint disease).

Exclusion criteria

BMI < 18 and > 35 Kg/m2

Contra-indications for exercise testing and prescription are on the basis of theanswers from the *physical activity readiness questionnaire* (PAR-Q) and familiarity(by self-report) of the following heart conditions: heart failure symptoms, myocardialinfarction less than three months before the start of the training program anddiagnosed with other cardiac diseases

Participants taking beta-blockers for the duration of the intervention.

Diagnosed with other neurologic or cachectic diseases or major surgery that may interfere with muscle quality (i.e. multiple sclerosis, ongoing cancer treatment or radiotherapy/ chemotherapy in the previous 6 months).

Participating in another regular and intense (> 2 times a week) physical training programme within 2 months prior to enrolment.

Ligament/muscle tear and/or other injuries within 6 months.

Taking drugs (e.g. performance enhancing drugs) or nutritional supplements (e.g. protein powder) known to increase muscle mass.

Inability to be scheduled for exercise therapy

Insufficient comprehension of Dutch language or no informed consent.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2024
Enrollment:	69
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	28-01-2025
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL86908.018.24