Aus dem Institut für Kreislaufforschung und Sportmedizin, der Deutschen Sporthochschule Köln

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Untersuchungen zum Einfluss von körperlicher Aktivität auf die Stoffwechselsituation von postmenopausalen Frauen

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Publikationen der Dissertation

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5. Effects of endurance training on thyroid response in pre- and postmenopausal women.
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Zusammenfassung

Die Menopause geht mit verschiedenen körperlichen Veränderung (Gewichtszunahme, Muskelmasseverlust) und Erkrankungen (Metabolisches Syndrom, Osteoporose) einher. Dies wirkt sich negativ auf die Lebensqualität der Frauen aus und belastet das Gesundheitssystem. Bestehende Trainingsempfehlungen basieren überwiegend auf Untersuchungen an Männern oder jungen Frauen. Zudem fokussieren diese sich häufig lediglich auf ein Symptom. Trotz Training berichten Frauen von Gewichtszunahme, Kraftlosigkeit, Gelenkbeschwerden und erhöhten Blutfettwerten. Die Trainingsempfehlungen scheinen bei postmenopausalen Frauen nicht zu greifen. Daher wurden in der vorliegenden kumulativen Dissertation während einer einmaligen Ausdauerbelastung die Reaktion des Stoffwechsels mittels Spiroergometrie bei prä- und postmenopausalen Frauen mit vergleichbarem BMI analysiert. Aufbauend darauf wurden zwei drei-monatige Trainingsintervention, bestehend aus Ausdauer- (2x/Woche) und Krafttraining (1x/ Woche), sowie Schlingentraining (3x/ Woche), in Kombination mit einer Protein/ Kohlenhydrat Supplementation durchgeführt und analysiert. Positive Effekte zeigten sich in der funktionellen Kraftfähigkeit, der Körperzusammensetzung und dem Körpergewicht. Die Supplementation verstärkte die Effekte leidglich bei der Rumpfkraft. In einer Subgruppenanalyse von 26 Probandinnen wurde mittels Isotopenalyse das $^{44}Ca/^{42}Ca$ Verhältnis gemessen und so der Effekt auf den systemischen Knochenstoffwechsel untersucht. Ein signifikanter Trainingseffekt war nachweisbar, obwohl das Training nicht speziell zur Verbesserung des Knochenstoffwechsels konzipiert war. Ergänzend wurde die Wirksamkeit eines reinen Krafttraining, mit freien Gewichten in zwei Intensitätsstufen, überprüft. Es zeigte sich eine signifikante Kraftsteigerung, die Körperzusammensetzung änderte sich hingegen nicht.

In einer Pilotstudie wurde die Reaktion der Schilddrüse nach akuten und chronischen Ausdauerinterventionen analysiert. Bei den postmenopausalen Frauen zeigte sich im Vergleich zu den prämenopausalen Frauen keine gesteigerte TSH Ausschüttung nach einem akuten Ausdauerreiz. Durch das Ausdauertraining wurde die Reaktion reduziert. Zusammenfassend kann ein Ausdauer- und Krafttraining zur Verbesserung der Kraftfähigkeit, der Körperzusammensetzung und dem Knochenstoffwechsel der postmenopausalen Frau empfohlen werden. Dennoch sind weitere Studien nötig um allumfassende Trainingsempfehlungen geben zu können.

Abstract

Menopause is accompanied by various physical changes (weight gain, loss of muscle mass) and diseases (metabolic syndrome, osteoporosis). This has a negative impact on women's quality of life and also places a burden on the healthcare system. Existing training recommendations are mainly based on studies of men or young women. Moreover, they often focus only on one symptom. Despite exercise, women report weight gain, lack of strength, joint problems and elevated blood lipids. Exercise recommendations do not appear to be effective in postmenopausal women. Therefore, in the present cumulative dissertation, metabolic response was analyzed by spiroergometry in pre- and postmenopausal women of comparable BMI, while a single endurance exercise. Based on this, two three-month training interventions, consisting of endurance training (2x/week) and strength training (1x/week), as well as sling training (3x/week), in combination with protein/carbohydrate supplementation were performed and analyzed. Positive effects were seen in functional strength, body composition and body weight. The supplementation promotes the effects in trunk strength. In a subgroup analysis of 26 female subjects, the $^{44}Ca/^{42}Ca$ ratio was measured by isotope analysis to investigate the effect on bone metabolism. A significant training effect was detectable, although the training was not specifically designed to improve bone metabolism. In addition, the efficacy of strength training alone, with free weights at two intensity levels, was examined. There was a significant increase in strength, but no change in body composition. In a pilot study, the thyroid response was analyzed after acute and chronic endurance interventions. Postmenopausal women did not show increased secretion of TSH after an acute endurance stimulus compared to premenopausal women. Endurance training reduced the response.

In conclusion, endurance and strength training can be recommended to improve strength capacity, body composition and bone metabolism in postmenopausal women. Nevertheless, further studies are needed to provide overall training recommendations.

Abkürzungsverzeichnis

postF	postmenopausale Frauen
präF	prämenopausale Frauen
RQ	Respiratorischer Quotient
WHO	World Health Organization
ACSM	American College of Sports Medicine
E2	17β-Estradiol
CVD	kardiovaskuläre Erkrankungen
metS	metabolisches Syndrom
M.	muculus
Mm.	musculi
BIA	Bio Impedanz Analyse
SD	Standardabweichung
PCA	Principal component analysis
LME	linear gemischte Modelle
TS	Trunk strength
LS	Limb Strength
IG	Interventionsgruppe
CG	Kontrollgruppe
BMB	Bewegungsmenge
BMD	Knochendichte
DXA	Dual-Energy-Röntgenabsorptiometrie
BM	Knochenstoffwechsel
MM	Muskelmasse
MI-RT	Mittlere Intensität Widerstandstraining
FFM	Fettfreie Masse
FM	Fettmasse
VL	Vastus lateralis
RF	Rectus femoris
TB	Triceps brachii
1RM	1 Wiederholungsmaximum

RT	Widerstandstraining
TSH	Thyriodea stimulierendes Hormon
HRT	Hormonersatztherapie
HIIT	High Intensity Interval Training
d.h.	das heißt
MW	Mittelwert
SD	Standardabweichung
z.B.	zum Beispiel
bzw.	beziehungsweise
Ca	Kalzium
IRMS	Infrarot Massenspektrometrie

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1. Einleitung

Bei Frauen weltweit tritt die Menopause in der Regel zwischen dem 48. und 52. Lebensjahr ein [1]. In Deutschland befinden sich ca. 7,3 Millionen erwerbstätige Frauen in der Menopause [2] und suchen auf Grund von verschiedensten körperlichen Veränderungen und Symptomen die FrauenärztInnen auf. Dies führt zu einem Anstieg an Beratungs- und Behandlungsanlässen [3]. Ursache für die Konsultation sind z.B. Harninkontinenz, Osteoporose und Gebärmuttersenkungen, der am häufigsten verwendeten ICD-10 Schlüsseln bei einem Arztbesuch ist N95: „Klimakterischen Störungen“ [3]. Dies zeigt, dass Frauen unter den Symptomen oder sogar Erkrankungen die mit der Menopause einhergehen leiden. Untersuchungen aus Großbritannien zeigen, dass sich ein Großteil der Frauen durch die Beschwerden bei der Arbeit belastet fühlen [4]. Einschränkungen am Arbeitsplatz haben neben den individuellen Folgen für die Frauen auch sozioökonomische Folgen. Betroffenen Frauen mit geeigneten Maßnahmen bzw. Therapien zu unterstützen, die den Umgang mit der Menopause erleichtern, stellt daher eine Notwendigkeit und Hilfestellung dar. Neben den belastenden Symptomen wie Hitzewallungen, nächtlichem Schwitzen und Stimmungsschwankungen [1,5], hat die Menopause aber noch schwerwiegendere Folgen wie Osteoporose und einen Anstieg des kardiovaskulären Risikos [6–8]. Weiterhin steigt die Zahl der Myokardinfarkte und Schlaganfällen nachweislich deutlich mit der Menopause an [9,10]. Als weitere Folge bedingt der 17β-Estradiol (E2) Mangel Veränderungen im Fettstoffwechsel die zur Gewichtszunahme, Steigerung des viszeralen Fettes besonders am Bauch und einer Steigerung der Blutfettwerte führen. Flankiert und gefördert wird dies durch einen Muskelmasseabbau der mit dem Alterungsprozess einhergeht [11–13]. Während in anderen Ländern z.B. in Großbritannien die Hormonersatz Therapie (HRT) intensiv genutzt wird, versuchen in Deutschland, laut Dr. Katrin Schaudig, Präsidentin der Deutschen Menopause Gesellschaft, viele Frauen ohne Hormone durch die Wechseljahre zu kommen [14]. Hickey et al. sprechen sich beispielsweise gegen HRT und für eine „Normalisierung der Menopause“ aus [15]. Regelmäßige körperliche Bewegung und Ernährungsinterventionen haben sich in der Therapie und Prophylaxe von kardiovaskulären Erkrankungen und Osteoporose schon bewiesen [16,17]. Ebenso kann dem Muskelmasseverlust, der Zunahme an Fettmasse und der Insulinresistenz durch regelmäßige körperliche Aktivität entgegengewirkt werden [18–20]. Auch menopausale Symptome wie Muskel- und Gelenkschmerzen, Stimmungsschwankungen, Schlafstörungen und abnehmende körperliche Fitness lassen sich mit Training positiv beeinflussen [21]. Daher stellt regelmäßiges körperliches Training einen geeigneten Lösungsansatz dar [1]. Allerdings zeigt sich, dass viele Empfehlungen sehr allgemein gehalten sind [17], nur auf Daten von Männern beruhen oder sich nur mit einem Symptom der Menopause befassen [22–24]. Hinzu kommt, dass die menopausale Begleitsymptome wie Gelenkschmerzen, Muskelschmerzen, psychische Symptome, Harninkontinenz, Schlafstörungen und Osteoporose [1] regelmäßige körperliche Aktivität in und nach der Menopause erschweren. In den USA reduzieren Frauen in der Mitte ihres Lebens das regelmäßige Training um 40 % [25,26]. In Folge bewirkt die Abnahme der körperlichen Leistungsfähigkeit eine Verschlechterung der Lebensqualität [27]. Im Gegensatz dazu konnten Martin et al. zeigen, dass sich Training positiv auf die Lebensqualität auswirkt und höhere Trainingsumfänge auch mit einer deutlicheren Verbesserung der Lebensqualität einhergehen [28].

Basierend auf den oben beschriebenen Erkenntnissen und dem Mangel an nicht medikamentösen Empfehlungen für postF soll im Rahmen dieser Dissertation der Fettstoffwechsel unter Belastung, die Effekte verschiedener Trainingsinterventionen auf die Körperzusammensetzung, die funktionelle Kraftfähigkeit und den Knochenstoffwechsel sowie die Reaktion der Schilddrüsenhormone betrachtet werden.

2. Wissenschaftlicher Hintergrund

2.1 Menopause

In der Zeit vor der Menopause werden Frauen als prämenopausal bezeichnet, während der menopausalen Umbruchszeit als perimenopausal und nach der Menopause als postmenopausal. Als postmenopausal gelten Frauen, wenn die letzte Regelblutung mindestens ein Jahr zurück liegt. Ergänzend zu den in der Regel ausreichenden klinischen Zeichen können die Hormonwerte im Blut bestimmt werden [5]. Hier gelten < 32pg/ml 17β-Estradiol und 31,6 - 116,3 mlU/ml FSH (follikelstimulierendes Hormon) als postmenopausal (Labor Wisplinghoff, Köln). Das veränderte hormonelle Gleichgewicht der Frauen hat eine Vielzahl von Veränderungen, Symptomen (z.B. Zunahme der Fettmasse) bis hin zu Erkrankungen wie Diabetes mellitus Typ 2 und kardiovaskuläre Erkrankungen zur Folge [29]. Dies bedingt, dass die meisten Frauen diese Phase als sehr belastend empfinden. Darüber hinaus führen die Beschwerden und die Erkrankungen neben der reduzierten Lebensqualität der Frauen, zu einer enormen finanziellen Belastung des Gesundheitssystem [30,31]. In der Zeit vor der Menopause zeigen die Frauen unregelmäßige Blutungen, diese können, müssen aber nicht von verschiedenen Symptomen begleitet werden. Zu den möglichen Symptomen zählen: Vasomotorische Symptome (Hitzewallungen, Schweißausbrüche), Schlafstörungen, Niedergeschlagenheit, Stimmungsschwankungen, Ängste, sexuelle Probleme und Gelenkbeschwerden [1,5]. Die zunächst unregelmäßigen und später manifestierten Symptome lassen sich auf eine veränderte Funktion der Hypothalamus-Hypophysen-Ovarien-Achse zurückführen. Vor der Menopause reguliert der Hypothalamus über die pulsatile Abgabe des glandotropen Releasing Hormon (Gn-RH) an die Hypophyse die Freisetzung der Gonadotropine. So regulieren das luteinisierende Hormon (LH) und das follikelstimulierende Hormon (FSH) die Sexualhormone Östrogen, Gestagen und Testosteron. Ebenfalls wird hier das thyreoideastimulierende Hormon (TSH) freigesetzt. Das Östrogen (17β-Estradiol) wird dann in den Ovarien gebildet und hier auch freigesetzt [32,33]. Wenn keine Eizellen mehr vorhanden sind, verringert sich die Estradiol und Inhibin Sezernierung in den Ovarien, die Folge ist das dadurch reduzierte bzw. ausbleibende Feedback an die Hypophyse und den Hypothalamus. Entsprechend des Regelkreises kommt es zu einer ausbleibenden Hemmung des Hypothalamus an die Hypophyse (Abbildung 1). Daraus resultiert der Anstieg des FSH und des LH [1,34].

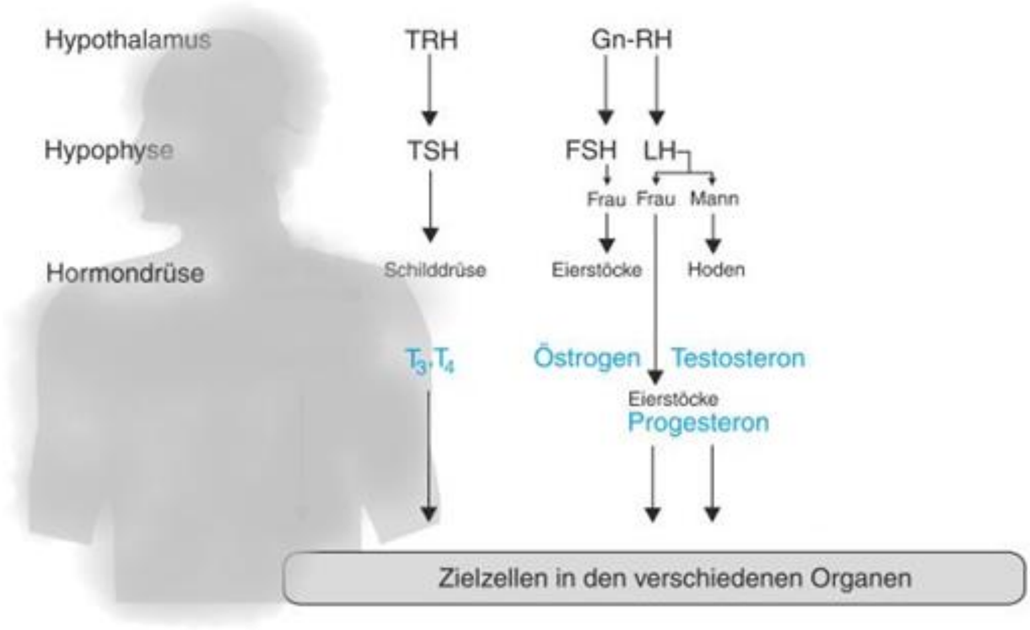

Abbildung 1: Regulationsketten der verschiedenen Hormone mit den dazugehörigen Achsen
TRH: Thyreotropin-Releasing-Hormon; TSH: thyreoideastimulierendes Hormon; T_3 : Triiodothyronin; T_4: Thyroxin; . Gn-RH: Releasing Hormon der glandotropen Sexualhormone; FSH: follikelstimulierendes Hormon; LH: luteinisierendes Hormon; modifiziert nach [32]

Während die Symptome zu Beginn, durch die kompensatorischen Mechanismen des weiblichen Körpers nur sehr unregelmäßig auftreten, manifestieren sich diese, wenn keine Eizellen mehr vorhanden sind und die Arbeit der Eierstöcke erloschen ist [33]. Zu diesem Zeitpunkt zeigt sich beispielsweise auch die nachweisbare Abnahme der Knochendichte [35]. Ebenfalls gehen mit dem Alter Veränderungen im Schilddrüsenhormonhaushalt einher. Erkrankungen und Störungen nehmen gerade bei Frauen in der Perimenopause zu [36,37].

2.2 Folgen und Symptome

Das veränderte Zusammenspiel der Hypothalamus-Hypophysen- Ovarien- Achse löst bei den Frauen vielfältige physische wie psychische Veränderungen aus [1,15,34,38–40]. Die deutlichste Veränderung ist das dauerhafte Ausbleiben der monatlichen Blutung und das Ende der Fortpflanzungsfähigkeit. Bei der aktuellen Lebenserwartung von Frauen in den Industrieländern folgt für die Frauen nun mehr als 1/3 ihrer Lebenszeit im postmenopausalen Zustand [41–43]. Die körperlichen Veränderungen belasten die Frauen beispielsweise durch die Abnahme der Libido oder eine Gewichtszunahme auf der einen Seite, auf der anderen Seite kommt es zur Manifestation von Krankheiten, wie z.B. Osteoporose und Herz-Kreislauf

Erkrankungen. Durch körperliche Aktivität können die menopausalen Symptome gelindert werden [44]. Sternfeld et al. konnten zeigen, dass sich vermehrte körperliche Aktivität, sowohl Sport als auch ein aktiver Lebensstil, vor der Lebensmitte, als auch eine Steigerung der körperlichen Aktivität ab der Lebensmitte sehr positiv auf die menopausalen Beschwerden und besonders auf die Gewichtszunahme auswirken [45]. Ebenso führt die körperliche Aktivität zu einer verbesserten Lebensqualität [25].

2.3 Abnahme der Muskelmasse

Die Abnahme der Muskelmasse ist ein typisches Symptom des Älterwerdens, welches durch die Menopause verstärkt wird [11–13]. Die Abnahme der Muskelmasse ist vorranging auf ein Missverhältnis zwischen Muskelprotein Synthese und Muskelprotein Abbau, sowie einen Anstieg von katabolen Effekten wie Stress und Entzündungen zurückzuführen [46–48,27]. Ergänzend dazu wirkt der Östrogenmangel positiv auf die Apoptose der Skelettmuskelzellen [48] (Abbildung 2). Die Reduktion von körperlicher Aktivität und Bewegungsmangel fördern diesen katabolen Effekt und können zur Entwicklung von Sarkopenie, Stürzen oder sogar die des Frailty Syndrom beitragen [46,48].

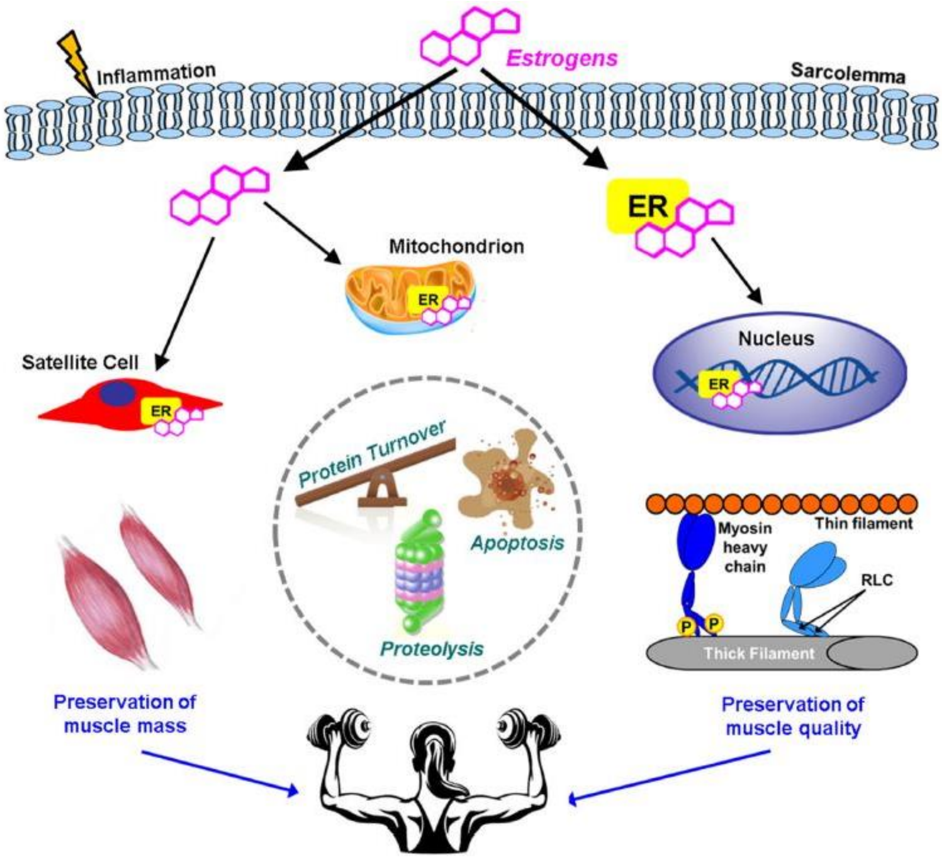

Abbildung 2: 17β- Estradiol Einfluss auf die Muskelkraft von Frauen.ER: Estrogen Rezeptor; aus [48]

Sjöblom et al. konnten zeigen, dass es eine enge Verbindung zwischen Sarkopenie, Osteoporose, Stürzen und Knochenbrüchen gibt. Besonders die reduzierte Handgriffkraft ist ein deutliches Zeichen für Sarkopenie und steht im direkten Zusammenhang mit den anderen oben genannten Effekten [49]. Das kombinierte Auftreten von Sarkopenie und Osteoporose wird als Osteosarkopenie bezeichnet. Die Prävalenz bei postmenopausalen Frauen ist hoch [50]. Neben Fehl- und Unterernährung, Erkrankungen und Veränderungen im hormonellen System, ist Immobilität und körperliche Inaktivität ein Hauptgrund für die Entwicklung der Sarkopenie [51]. Da ältere Menschen im Vergleich zu Jüngeren weniger körperlich aktiv sind und die tägliche Zeit, die mit Sport verbracht wird mit dem Alter abnimmt, erhöht sich die Wahrscheinlichkeit an Sarkopenie zu erkranken [52]. Bei Nagern konnte gezeigt werden, dass 17β-Estradiol den Bewegungsantrieb der Tiere fördert, während ein Mangel zu einer Reduktion der Bewegung und somit zu einer Gewichtszunahme führt [53,24]. Dieser direkte Zusammenhang konnte bisher bei postmenopausalen Frauen nicht nachgewiesen werden. Dennoch kommt es durch die Veränderung des spontanen Bewegungsverhaltens und der Essgewohnheiten [54] zur Abnahme an körperlicher Leistungsfähigkeit [55,56]. Ergänzend dazu kommt es zur Akkumulation von viszeralem Fett, einer androgenen Fettverteilung und zur Abnahme der Muskelmasse [57]. Ein Erhalt und ein lebenslanges Training der Muskulatur scheint daher für die Gesunderhaltung von postmenopausalen Frauen essenziell.

2.4 Prophylaxe und Therapie bei der Abnahme der Muskelmasse

Die American Heart Association und das American College of Sports Medicine (ACSM) empfehlen mindestens 30 Minuten moderate aerobe Belastung an fünf Tagen pro Woche oder 20 Minuten intensive aerobe Belastung an drei Tagen pro Woche. Die Empfehlung für Krafttraining lautet an zwei nicht aufeinanderfolgenden Tagen pro Woche acht bis zehn Übungen für die Hauptmuskelgruppen (Bauch, Arme, Beine, Hüften, Schulter) mit 10 bis 15 Wiederholungen [58–60]. Progressiv gestaltetes Krafttraining gegen Widerstände z.B. an Kraftgeräten oder mit Bändern zeigt positive Effekte, hier scheint die wöchentliche Steigerung der Wiederholungen bei postmenopausalen Frauen als besonders effektiv [61]. Die WHO empfiehlt ebenfalls neben dem moderaten aeroben Training von 150-300 Minuten mindestens zweimal pro Woche Krafttraining für alle großen Muskelgruppen zum Erhalt der Gesundheit [17]. Thomas et al. konnte zeigen, dass Ganzkörper Krafttraining mit zwei bis drei

Einheiten pro Woche mit sieben bis acht Übungen und 9-16 Wiederholungen bei älteren Frauen zu einer Steigerung der Muskelmasse führt - allerdings zu keiner Reduktion der Fettmasse [62]. Viecelli et al. konnten zeigen, dass bei untrainierten Erwachsenen das Trainingsvolumen am besten über eine Erhöhung der Wiederholungen, der Sätze oder der Trainingshäufigkeit erfolgt [63]. Dabei sollten 24-48 Stunden Pause zwischen den einzelnen Trainingseinheiten liegen. Es sollten alle Formen der Muskelanspannung (konzentrisch, isometrisch und exzentrisch) angewendet werden und das vollständige Bewegungsausmaß (ROM) genutzt werden. Bei einer niedrigen Intensität (<50% des 1RM) sollte bis zum Muskelversagen trainiert werden, um eine optimale Hypertrophie zu erreichen [63,64]. Um dem Auftreten der Osteosarkopenie entgegenzuwirken, werden ebenfalls “lifestyle” Interventionen bestehend aus Krafttraining, Protein-, Vitamin D-, Calcium- und Kreatinsupplementation empfohlen [65,66]. Dass sich eine Kombination aus Krafttraining und Ausdauertraining auf dem Laufband positiv auf die Muskelkraft, die Hämodynamik und die arterielle Steifigkeit auswirkt, konnten Figueroa et al. zeigen [67].

2.5 Veränderungen Fettstoffwechsel

Neben der Abnahme der Muskelmasse kommt es durch das abnehmende bzw. fehlende 17β-Estradiol (E2) zur Zunahme des viszeralen Fettgewebes [68,69]. Diese verstärkte Akkumulation von Fettgewebe ist meist diätunabhängig [23]. Zusätzlich verschiebt sich die Fettanlagerung von der subkutanen Anlage in der Gesäß- und Hüftregion hin zum viszeralen Fettakkumulation am Bauch. Studien zeigen, dass Frauen über einen Zeitraum von 3 Jahren um die Lebensmitte 2-2,5 kg zunehmen. Der Taillen-Umfang steigert sich im gleichen Zeitraum um 2,2 cm [59,70,71]. Die vermehrte, androgene Anlagerung wirkt sich negativ auf die kardiovaskuläre Gesundheit der Frauen aus. Die Sterblichkeit, das Risiko für Herz-Kreislauf-Erkrankungen und die Wahrscheinlichkeit am Metabolischen Syndrom zu erkranken nimmt zu [6–8]. Anhand von Untersuchungen an Nagern und an Frauen unter Hormonersatztherapie zeigt sich, dass die Fettsäurenoxidation im Muskel bei Frauen deutlich ansteigt und dass ovariektomierte Nager deutliche Einbußen in der Fähigkeit zeigen, Fette zu oxidieren [72,73]. Zusätzlich zeigten ovariektomierte Nager proinflammatorische Zustände im viszeralen Fettgewebe [74]. Die oben beschriebene Abnahme der Muskelmasse hat zudem zur Folge, dass es zu einer Abnahme des

Grundumsatzes der Frauen kommt, da die fehlenden Muskeln nicht mehr mit Energie versorgt werden müssen [75,41]. Die Fettoxidation wird durch den zunehmenden Muskelabbau deutlich eingeschränkt, wohingegen die Lipolyse des Fettgewebes nahezu uneingeschränkt bleibt [76–78]. Dies wirkt sich verstärkend auf die Gewichtszunahme aus. Die Muskelmasse beeinflusst als stoffwechselaktives Gewebe [79] den menschlichen Metabolismus stark, daher stehen altersbedingte Stoffwechselerkrankungen wie beispielsweise Diabetes mellitus Typ 2 und das metabolische Syndrom in einer engen Verbindung mit der abnehmenden Muskelmasse [62]. In Untersuchungen konnte gezeigt werden, dass das Fehlen von 17β-Estradiol zu einer reduzierten Adipozyten-Lipoprotein-Lipasen Aktivität unter körperlicher Belastung führt. Diese reduzierte Adipozyten-Lipoprotein-Lipasen Aktivität führt dazu, dass weniger Triglyceride und freie Fettsäuren als Energielieferant zur Verfügung stehen [80]. Die Folge ist eine reduzierte Fettoxidationsrate im gesamten Körper, diese geht laut Abildgaard et al. mit einem hohen Anteil an viszeralem Fett und einer niedrigen Insulinsensitivität einher. Dies könnte die Vorstufe zur Entwicklung metabolischer Erkrankungen sein [81]. Bei Nagern und bei Menschen konnte ein Einfluss des E2 auf den Appetit aufgezeigt werden, so scheinen durch E2 Appetit und Nahrungsaufnahme reduziert zu werden [73,82,83]. Demgegenüber fördert Testosteron den Appetit und die Nahrungsaufnahme [73]. E2 schützt die Zelle und hier besonders die Mitochondrien vor oxidativem Stress - auch dieser Schutz geht verloren und beeinflusst dann den Stoffwechsel negativ [82]. Der verändertere Fettmetabolismus zeigt sich an verschlechtern Blutfettwerten (Triglyceride steigen, Cholesterin steigt, High Density Lipoprotein nimmt ab, Low Density Lipoprotein steigt) [41], ebenso steigt das Risiko für eine Insulinresistenz und der Glukose Stoffwechsel wird gestört [84,85]. Die hohe Lipolyserate im viszeralen Fett bedingt viele freie Fettsäuren. Diese überschwemmen die Leber und führen so zu einer hepatischen Insulinresistenz [41]. Somit hat die veränderte Fettanlagerung neben dem Einfluss auf das Wohlempfinden und die Lebensqualität auch einen massiven Einfluss auf den Energiehaushalt und die Gesundheit von postmenopausalen Frauen [86]. Das Atherosklerose Risiko steigt an, kardiovaskuläre Erkrankungen wie beispielsweise Myokardinfarkte, arterielle Hypertonie und Schlaganfälle nehmen zu [9,10]. Im Vergleich dazu haben prämenopausale Frauen ein niedrigeres Risiko und eine geringere Inzidenz von kardiovaskulären Krankheiten als gleichaltrige Männer. Leider ändert sich das massiv mit dem Einsetzten der Menopause [23,87].

2.6 Prophylaxe und Therapie bei den Veränderungen des Fettstoffwechsels

Regelmäßige körperliche Aktivität, gesunde Ernährung und Gewichtsnormalisierung stellen Lösungen dar. Besonders moderates Ausdauertraining scheint wie bei jüngeren Menschen geeignet, da die Triglycerid Speicher geleert werden, um ausreichend Energie für die Muskulatur bereitzustellen [76]. Ko et al. verweisen ebenfalls auf die Notwendigkeit die freien Fettsäuren im Blut zu eliminieren, um eine Insulinresistenz zu vermeiden [41]. Cheng et al. konnten in einer Übersichtsarbeit zeigen, dass Trainingsinterventionen in Kombination mit diätetischer Intervention die größten Effekte zeigten und die Frauen das Körpergewicht reduzierten, Fettmasse verloren und Muskelmasse aufbauten [88]. Reine Trainingsinterventionen reduzierten zwar das Körpergewicht, zeigten aber keine Reduktion der Fettmasse, ebenso bei reinen Diäten [88]. Bei übergewichtigen postmenopausalen Frauen sollte eine Diät mit Kalorienrestriktion angewendet werden, dabei sollte aber auf die ausreichende Versorgung mit Proteinen geachtete werden. Es werden 0,8g/kg/Tag empfohlen, um dem Risiko der Sarkopenie entgegenzuwirken, die Diät sollte dann mit Training zum Muskelaufbau kombiniert werden [41]. Asikainen et al. empfehlen täglich mindestens 30 Minuten Walking Training und zweimal pro Woche Krafttraining [89]. Das Krafttraining sollte bei 40% des 1RM starten, alle großen Muskelgruppen beanspruchen, aus acht bis zehn Übungen mit jeweils acht bis zehn Wiederholungen bestehen. Ergänzt werden sollte das Programm durch eine Diät . Den positiven Effekt von Krafttraining an Geräten auf die Blutfettwerte und das viszerale Fett konnte Nunes et al. zeigen. Die Frauen erhöhten die Muskelkraft und reduzierten die Fettmasse. Zudem reduzierte sich das Gesamtcholesterin und das LDL im Blut. Ebenso verloren die Frauen an Bauchumfang. Da dort sowohl mit einem hohen als auch einem niedrigen Trainingsvolumen trainiert wurde, kamen die Autoren zu dem Schluss, dass sich beide Trainingsformen eignen, um Muskelkraft und Körperzusammensetzung positiv zu beeinflussen, die Indikatoren für das Bauchfett (Bauchumfang, Waist to Hip ratio) und die Entzündungsindikatoren wie IL-6 sich aber besser durch ein hohes Volumen beeinflussen lassen [90]. Batacan et al. empfehlen dreimal pro Woche ein HII- Training, um das kardiovaskuläre Risiko zu minimieren. Einfluss hat das HIIT auf das Körperfett, den Taillenumfang, Herzfrequenz und Nüchternglucose. Das Training ist deutlich zeitsparender als moderates normales Training in der Dauermethode [91], zusätzlich ist es effektiver, um die Fettmasse zu reduzieren [92]. HIIT in Kombination mit Krafttraining führt zusätzlich zu einer Steigerung der Muskelmasse [91]. Dies erweist sich in Anbetracht des Sarkopenie Risikos als sehr zielführend. Das sich ein kombiniertes Training aus Ausdauertraining (Walking) und funktionellem Krafttraining mit Kleingeräten in Form eines Zirkeltrainings positiv auf die Körperzusammensetzung und die funktionelle Fitness bei postmenopausalen Frauen auswirkt, zeigten Neves et al. [93]. Den positiven Effekt eines kombinierten Krafttrainings an Geräten und einem Ausdauertraining (Walking) im Vergleich zu einem HII-Training zeigten Nunes et al. [94]. In beiden Gruppen konnte das Körperfett und das viszerale Bauchfett reduziert werden. Allerdings war die Reduktion des viszeralen Bauchfettes in der HIIT Gruppe größer. Somit scheint das zeitsparende HIIT eine gute Alternative, vor allem für stark beschäftigte Frauen zu sein. In der Untersuchung wurde das Körpergewicht, die Fettmasse allgemein, die Fettmasse am Rumpf reduziert und die Muskelmasse an den Beinen gesteigert [94]. Eine weitere mögliche Therapie stellt die Hormonersatz Therapie (HRT) dar. Diese geht allerdings aber auch mit erheblichen Nebenwirkungen einher [95]. Dennoch zeigt die HRT bei Frauen eine deutliche Verbesserung der Fettoxidation, weniger viszerale Fettmassezunahme und weniger Fettakkumulation am Bauch [96].

2.7 Osteoporose

Eine weitere Folge der Menopause ist die Osteoporose. Hierbei kommt es zu einem verstärkten Knochenabbau. E2 wirkt vor der Menopause protektiv auf den Knochen, in dem es die Aktivität der Osteoklasten fördert [97] mit der Abnahme des E2 geht dieser Schutz verloren [98]. Daraus resultiert eine höhere Prävalenz und Inzidenz, da der altersbedingte und der durch die Menopause ausgelöste Knochenverlust zusammen treffen [99,100]. Frauen verlieren während der gesamten menopausalen Umstellung zwischen 40% und 60% der Knochenmasse [100]. Häufig geht dies mit Frakturen, Krankenhausaufenthalten und Immobilität einher. Laut Hadji et al. erleiden über die Hälfte der an Osteoporose erkrankten Frauen innerhalb von 4 Jahren nach Diagnosestellung eine Knochenfraktur [101]. Zurückzuführen ist dies neben einer niedrigere Knochenmasse auf eine mikroarchitektonische Verschlechterung des Knochengewebes. Frakturen der Wirbelkörper treten bei Alltagsbelastungen auf und führen zu Schmerzen und Immobilität. Dem gegenüber werden Frakturen der Hüfte oder des Radius oft durch Stürze ausgelöst. Neben Krankenhausaufenthalten haben diese ebenfalls eine eingeschränkte Mobilität zur Folge [102]. Aus der Osteoporose und deren Folgen resultieren eine deutliche Abnahme der Lebensqualität der Frauen und direkte sowie indirekte Kosten für das Gesundheitssystem [95,103,104].

2.8 Prophylaxe und Therapie bei Osteoporose

Regelmäßiges körperliches Training, eine gesunde Ernährung, eine ausreichende Versorgung mit Vitamin D und der Verzicht auf Alkohol und Nikotin werden präventiv und therapeutisch empfohlen [98,100]. Dynamisches Krafttraining gilt als ein wichtiger Aspekt zur Vorsorge und Behandlung von Osteoporose [105]. Das Training sollte langfristig erfolgen. Es kann mit freien Gewichten durchgeführt werden, was zum einen kostengünstig ist aber auch den Zugang für alle Personengruppen ermöglicht. Ebenso können bereits bestehende körperliche Einschränkungen berücksichtigt werden [106,107]. Die Trainingsfrequenz sollte maximal zwei Einheiten pro Woche betragen, bei der Intensität gibt es keine einheitlichen Angaben. So konnten Shojaa et al. keine Überlegenheit von hoch intensiver gegenüber moderater oder niedriger Trainingsintensität finden. Andere Autoren zeigen aber die Überlegenheit von hochintensivem Training auf [108,109]. Es scheint, dass die unterschiedlichen Trainingsarten an unterschiedlichen Stellen im Skelettsystem wirken. Ein Training, das aus vielen unterschiedlichen Belastungsarten besteht, scheint die Knochendichte in den Wirbelkörpern zu verbessern, während progressiv gestaltetes Krafttraining mit Widerständen die Knochendichte im Bereich des Oberschenkelhalses verbessert [100,110,111]. Allerdings sollte berücksichtigt werden, dass in der Regel auch nur diese zwei Regionen untersucht werden und nicht der gesamte Knochenstoffwechsel betrachtet wird [112]. Demnach scheinen kombinierte Trainingskonzepte bestehend aus der Nutzung von Bodenreaktionskräften (Walking) und Gelenkbewegungen gegen Widerstände am effektivsten [113]. Neben dem Training wird eine ausreichende Versorgung mit Calcium, Vitamin D und Proteinen über die normale Ernährung oder wenn dies nicht möglich ist als Supplementation, empfohlen. Neben 1200 mg Calcium und 800 IU Vitamin D scheinen 1,2 g Proteine pro kg Körpergewicht pro Tag zielführend zu sein [100].

2.9 Supplementation von Proteinen und Kohlenhydraten

Aminosäuren spielen eine entscheidende Rolle bei der Muskelprotein Synthese. Studien zeigen große Effekte bei älteren Erwachsenen [114–116]. Zudem zeigten Studien, dass sich die Protein Supplementation positiv auf die Muskelmasse, -kraft und Muskelfunktion von älteren Menschen auswirkt [117,79]. Dabei scheint die kombinierte Gabe aus Proteinen und Kohlenhydraten der isolierten Proteingabe überlegen [118]. Dies ist auf die insulintrope Wirkung von Aminosäuren wie Leucin zurückzuführen. Diese sorgt durch eine vermehrte Ausschüttung von Insulin aus der Bauchspeicheldrüse für eine höhere Glukoseaufnahme in die Muskelzellen [119] in Kombination mit einer stimulierten Muskelprotein Synthese [120]. Zudem scheinen trainingsinduzierte Muskelschäden durch die kombinierte Supplementation geringer auszufallen [121,122]. Proteine trierischen Ursprungs fördern die Muskelprotein Synthese stärker als pflanzliche [116]. Um die Glykogenspeicher schnell wieder aufzufüllen empfiehlt die International Society of Sports Nutrition (ISSN) für trainierende Erwachsene die kombinierte Aufnahme von 0,8 g/kg/h Kohlenhydraten und 0,2-0,4 g/kg/h Proteinen. Für die Aufnahme beim Krafttraining der Hauptmuskelgruppen mit drei bis sechs Sätzen und 8-12 Wiederholungen, werden Kohlenhydrate alleine oder in Kombination mit Proteinen empfohlen. Dies füllt die Glykogenspeicher auf, mildert Muskelschäden und erleichtert die Trainingsanpassung. Eine Supplementation während oder nach dem Sport mit Kohlenhydraten und Proteinen fördert den Kraftzuwachs und verbessert die Körperzusammensetzung. Zudem kann durch die Supplementation von Proteinen innerhalb von 2 Stunden nach Trainingsende die Muskelprotein Synthese gefördert werden [123]. Isenmann et al. zeigten, dass sich durch eine Protein/Kohlenhydrate Supplementation, bestehend aus Sauermilchkäse und Weißbrot, innerhalb von 30-Minuten nach dem Training, die Regenerationsfähigkeit junger Erwachsener deutlich verbessert. Die funktionelle Leistung der Studienteilnehmer, die Muskelschädigungsmarker und Entzündungsparameter wurden positiv beeinflusst [124,125].

3. Zielsetzung

Basierend auf den oben dargestellten enormen persönlichen und ökonomischen Belastungen, die die Menopause bei den betroffenen Frauen bewirkt, hat diese kumulative Dissertation das Ziel, die Wirkung von Training auf den Organismus der postmenopausalen Frau zu analysieren und darauf aufbauend Empfehlungen zur Linderung der Symptome und die Gesunderhaltung der Zielgruppe zu geben. Zudem sollen Empfehlungen, die auf Untersuchungen an Männer und jungen Frauen beruhen an der postmenopausalen Zielgruppe überprüft werden und so diese wissenschaftliche Lücke geschlossen werden.

Dazu sollen zum einen Erkenntnisse über die physiologische Reaktion des postmenopausalen Organismus auf einen akuten Trainingsreiz hin analysiert werden. Zum anderen sollen verschiedene Trainingsformen und deren Effekt auf die Körperzusammensetzung, die funktionelle Kraftfähigkeit, den Knochenstoffwechsel und die Auswirkung auf die Schilddrüsenhormone (TSH, fT4, fT3) betrachtet werden. Dabei liegt der Fokus auf den Effekten einer kombinierten Trainingsintervention (Ausdauer- und Krafttraining) mit Protein/Kohlenhydrat Supplementation auf die Kraftfähigkeit, die Körperzusammensetzung und den Knochenstoffwechsel. Vorbereitend dazu wird die Reaktion des postmenopausalen Energiestoffwechsel auf eine akute Belastung hin analysiert. Ergänzend zu dem kombinierten Training, werden die Effekte eines Krafttrainings dargestellt. Im Hinblick auf den Hormonhaushalt und die häufig mit der Menopause einhergehenden Veränderungen der Schilddrüsenhormone, folgt ein kurzer Exkurs zur Reaktion der Schilddrüsenhormone auf ein akutes und ein chronisches Ausdauertraining bei postmenopausalen Frauen.

Vor dem Hintergrund der dargestellten Forschungsziele sollen die folgenden Forschungsfragen beantwortet werden:

1. Welchen Einfluss hat eine akute, 30-minütige Ausdauerbelastung auf den Fettstoffwechsel von prä- und postmenopausalen Frauen mit vergleichbarem BMI?
2. Wie wirkt sich ein 3-monatiges Kraft- und Ausdauertraining in Kombination mit einer Protein/Kohlenhydrat Supplementation auf die Kraftfähigkeit und die Körperzusammensetzung von postmenopausalen Frauen aus?
3. Wie wirkt sich ein 3-monatiges Kraft- und Ausdauertraining in Kombination mit einer Protein/Kohlenhydrat Supplementation auf den Calcium Stoffwechsel des Knochens bei postmenopausalen Frauen aus?
4. Wie wirkt sich ein Krafttraining mit freien Gewichten und zwei unterschiedlichen Intensitätsstufen auf die Muskelkraft und die Körperzusammensetzung von Frauen mittleren Alters abhängig von ihren Hormonstatus (prä- und postmenopausal) aus?
5. Welchen Effekt hat eine akute Ausdauerintervention bei prä- und postmenopausalen Frauen und eine chronische Ausdauerintervention bei

postmenopausalen Frauen auf die Ausschüttung der Schilddrüsenhormone (TSH, fT4. fT3)?

4. Veröffentlichungen

Im folgenden Abschnitt werden die 5 Publikationen vorgestellt, die im Rahmen der vorliegenden Arbeit entstanden sind. Es werden ausschließlich die wichtigsten Erkenntnisse der einzelnen Untersuchung aufgeführt.

Alle Studienprotokolle wurden gemäß der Deklaration von Helsinki durchgeführt und von der Ethikkommission der Deutschen Sporthochschule Köln überprüft und genehmigt. Zudem wurde die Hauptstudie (DRKS-ID: DRKS00024144) (siehe 4.2, 4.3), die Krafttrainingsstudie (DRKS-ID: DRKS00023826) (siehe 4.4) und die Schilddrüsenstudie (DRKS-ID: DRKS00020425) (siehe 4.5) im deutschen Register für klinische Studien registriert. Detaillierte Beschreibungen über die Analyseverfahren der untersuchten Parameter und über die statistischen Auswertungen sind in den Original-Publikationen im Anhang zu finden.

4.1 Publikation 1: "Effects of Acute Aerobic Exercise on Fat Metabolism in Pre- and Postmenopausal Women of Comparable Body Mass Index" Deutsche Zeitschrift für Sportmedizin.2022; 73:235-240.doi:10.5960/dzsm.2011.541

Einleitung: Mit Einsetzen der Menopause steigt das Risiko für kardiovaskuläre Erkrankungen (CVD) wie Herzinfarkt, Arteriosklerose und Schlaganfälle an [43]. Ein Grund ist der durch die Estrogenabnahme veränderte Fettstoffwechsel (FS) [69]. Im Tierexperiment wurde gezeigt, dass E2 direkt den Fettstoffwechsel beeinflusst. Daraus resultiert die Notwendigkeit CVD´s und metabolische Erkrankungen bei postmenopausalen Frauen entgegenzuwirken. Körperliche Aktivität scheint ein gutes Mittel gegen die menopausalen Veränderungen zu sein. Ausdauertraining kann das Risiko für CVD reduzieren und sich positiv auf den FS auswirken. Das Ziel der Studie ist es, die Fettstoffwechselfähigkeit von prä- (präF) und postmenopausalen Frauen (postF) mit vergleichbarem BMI während einer akuten Ausdauerbelastung zu analysieren.

Methode: 12 präF (25,0±3.5 Jahre) und 12 postF (57,7±4.3 Jahre) wurden in die Studie eingeschlossen. Im Blut wurden die Parameter Triglyceride, LDL, HbA1C und Estradiol erhoben. Die anthropometrischen Daten und die Körperzusammensetzung wurden ermittelt. Während 30 Minuten (60% der 4mmol Schwelle) Dauerbelastung auf dem

Fahrradergometer wurde der Respiratorische Quotient (RQ), die Herzfrequenz erhoben und Blut zur Laktatanalyse aus dem Ohrläppchen entnommen.

Ergebnis: Während der Studie mussten 2 präF exkludiert werden. Bei den postF lag die letzte Regel 5 bis 7 Jahre zurück. Während der BMI der präF- und postF (23.0±2.3 prämenopausal; 23.6±1.3 postmenopausal) vergleichbar war, unterschieden sich Körperfett (KF) (p=0,001), Magermasse (p=0,001) und Bauchumfang (p=0,003) signifikant (Tabelle 1). Signifikante Gruppeneffekte konnten auch bei den Serumkonzentrationen von HbA1c (p=0,001), Cholesterin (p=0,001) und LDL (p=0,000) festgestellt werden (Tabelle 2).

Tabelle 1: Körperzusammensetzung
M= Mittelwert; SD= Standardabweichung; LBM= lean body mass; BCM= Körperzell Masse; BMI = Body mass Index

	prämenopausal (n=12)		postmenopausal (n=12)		
	M	*SD*	*M*	*SD*	*p-value*
Alter (Jahre)	25,0	3,5	57,7	4,3	0.001
Gewicht (kg)	67,6	9,1	64,1	4,9	0.378
BMI (kg/m2)	23,0	2,3	23,6	1,3	0.444
Bauchumfang (cm)	76,2	7,4	85,1	5,5	0.003
Fettmasse (%)	27,9	3,9	34,0	2,4	0.001
Magermasse (LBM)(%)	72,9	3,9	65,9	2,4	0.001
Körperzellmasse (BCM) (%)	27,6	3,2	21,9	1,5	0.001

Tabelle 2: Blutparameter
HbA1c= Hamoglobin A1c; TG = Triglyceride; CHOL = Cholesterin; HDL= high density lipoprotein; LDL= low density lipoprotein M= Mittelwert; SD= Standardabweichung

	prämenopausal (n=12)		postmenopausal (n=12)		
	M	*SD*	*M*	*SD*	*p-value*
Blutzucker [mg/dl]	90,7	4,9	98,7	6,2	0.002
HbA1c [%]	5,1	0,2	5,5	0,2	0.001
TG [mg/dl]	64,6	16,6	80,7	29,5	0.178
CHOL [mg/dl]	162,6	23,3	243,9	36,0	0.001
HDL [mg/dl]	59,5	9,2	7,9	12,5	0.007
LDL [mg/dl]	90,3	18,1	154,2	34,7	0.001

Gruppenunterschiede in der Laktatkonzentration unter Belastung 10, 20 und 30 Minuten nach Beginn konnten gemessen werden. Bei den präF steigt der Laktatwert in den ersten 10 Minuten an, blieb dann bis zur 20. Minute konstant und sank dann bis zur Minute 30. Bei den postF hingegen stieg das Laktat in den ersten 10 Minuten stark an und verharrte auf diesem hohen Niveau bis zum Ende der Belastung (Abbildung 3).

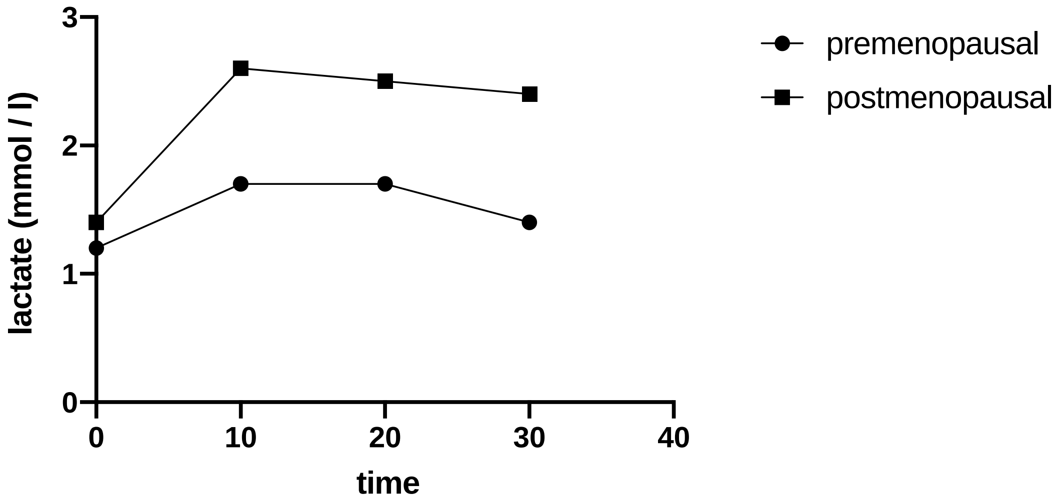

Abbildung 3: Originalabbildung: Laktatspiegel in mmol/l während einer 30-minütigen Belastung

Der RQ unterschied sich in Ruhe nicht und stieg in beiden Gruppen innerhalb der ersten 10 Minuten der Belastung deutlich an. Im Anschluss sank er über die folgenden 20 Minuten bei den präF ab, bei den postF (p=0,010) stieg dieser über die folgenden 20 Minuten weiterhin an (Abbildung 4).

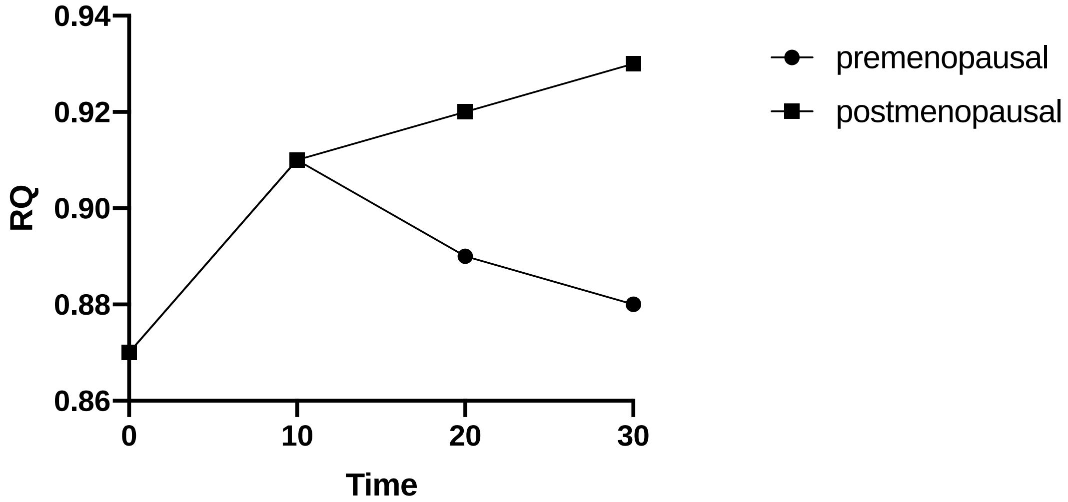

Abbildung 4: Originalabbildung: Respiratorischer Quotient (RQ) während der 30-minütigen Belastung

Diskussion: Der größere Bauchumfang, das Körperfett und die niedrige Magermasse der postF zeigen die Veränderung der Körperzusammensetzung durch die Menopause, wenn auch der BMI vergleichbar zur prämenopausalen Gruppe war. Eine Anhäufung von Fett, vor allem im Rumpfbereich, geht mit einer Zunahme von CVD bei postF einher, auch bei normalen BMI [126,127]. Die postmenopausalen Frauen zeigten signifikant höhere Blutzucker, HbA1c, Cholesterin, LDL und HDL Werte im Vergleich zu den prämenopausalen Probandinnen. Diese Veränderung konnten auch schon Pu et al. zeigen [128]. Der RQ in Ruhe zeigte keinen Unterschied zwischen den Teilnehmerinnen, der Anstieg bei beiden Gruppen innerhalb der ersten 10 Minuten kann mit einer vermehrten Nutzung von Kohlenhydraten als Energielieferant erklärt werden. Wie erwartet folgt bei einer moderaten, andauernden Belastung danach ein Absinken, da nun vermehrt Fette zur Energiebereitstellung verwendet werden. So fördert moderate Belastung bei präF die Lipolyse [129]. In der postmenopausalen Gruppe hingegen kommt es auch nach 30 Minuten zu keinem Absinken des RQ´s, es werden weiterhin Kohlenhydrate zur Energiebereitstellung verwendet. Daraus lässt sich ableiten, dass postF nicht in der Lage sind während 30 Minuten moderater Belastung den Fettstoffwechsel zu aktivieren. Somit scheint der Hormonstatus nicht nur die Blutfettwerte, sondern auch den Fettmetabolismus zu beeinflussen. Eine Erklärung könnte hier der direkte Einfluss des E2 auf die Mitochondrien Membran und deren Funktion sein [130,131]. Abildgaard et al. konnten zeigen das postF einen höheren RQ während 45 Minuten Ausdauerbelastung haben. Ebenso konnte gezeigt werden, das präF einen niedrigeren Körperfettanteil hatten, sowie die vorliegenden Studie zeigt [81]. Die dargestellten Daten zeigen, dass E2 eine entscheidende Rolle im Fettstoffwechsel spielt. Die veränderte Reaktion auf einen akuten und moderaten Belastungsreiz muss bei der zukünftigen Trainingsplanung und bei Trainingsempfehlungen für postF berücksichtigt werden. Der Alterseffekt muss hier kritisch hinterfragt werden, da die präF noch sehr jung und dementsprechend weit weg von der Menopause waren.

<u>Konklusion:</u> Es zeigt sich, dass postF im Vergleich zu präF einen veränderten Fettstoffwechsel aufweisen. Auf Grundlage dieser Erkenntnis müssen neue Trainingsempfehlungen für postF entwickelt und die bestehenden überdacht werden.

4.2 Publikation 2: ”Combinatory Effects of Training and Nutritive Administration of Carbohydrates and Protein via Food on Strength in Postmenopausal Women, and Old Men and Women.” Nutrients. 2023,15(6):1531.doi:10.3390/nu15061531

<u>Einleitung:</u> Der Alterungsprozess geht mit einer Vielzahl von physischen Veränderungen wie einer abnehmenden Muskelmasse und einem Anstieg an CVD´s einher. Bei Frauen spielt hierbei die Menopause eine entscheidende Rolle. Durch die Abnahme des E2 werden die Abnahme der Muskelmasse und die Entwicklung der

Sarkopenie gefördert [41,66,132]. Ebenso steigt das Risiko für Erkrankungen wie Diabetes mellitus Typ 2 oder das metS [41,133]. Es ist notwendig dem Muskelmasseverlust und der abnehmenden Kraft entgegenzuwirken, um die Entwicklung der altersbedingten Erkrankungen zu verhindern [64]. Viele Studien zeigen den positiven Effekt von regelmäßigem Training zur Prävention und Therapie. Verstärkt werden diese Effekte durch die Supplementation von Proteinen [27,134]. Es gibt zwei Ursachen für einen erhöhten Proteinbedarf. Zum einen eine unzureichende Ernährung im Alter und Situationen in denen z.B. durch intensives Training ein höherer Proteinbedarf entsteht. Häufig besteht bei postF kein direktes Proteindefizit, dennoch kann eine Proteinsupplementation die funktionelle Anpassung auf Grund eines Trainingsstimulus fördern [79]. Daher werden 20-25 g Protein nach dem Training empfohlen [135]. Studien haben gezeigt, dass die kombinierte Aufnahme von Proteinen und Kohlenhydraten zu einer höheren Glykogenspeicherung in der Skelettmuskulatur und einem stärkeren Anstieg des Blutzuckerspiegels und der Insulinkonzentration führt als bei einer reinen Kohlenhydratzufuhr [136]. Isenmann et al. verglichen die Aufnahme einer Protein/Kohlenhydrat-Kombination über Shakes und natürliche Lebensmittel direkt nach dem Training hinsichtlich der regenerativen Wirkung auf die Muskulatur. Die Ergebnisse zeigten, dass Shakes und die Supplementierung über eine natürliche Proteinquelle gleichermaßen Muskelschäden nach dem Training reduzieren konnte [124]. Lichtenberg et al. wiesen nach, dass ein Training mit einer Proteinsupplementierung durch Pulver bei sarkopenischen Senioren ebenfalls zu einem deutlichen Muskel- und Kraftzuwachs führte [137]. Der Verzehr von Milchprodukten und Weißbrot nach dem Training hat eine proregenerative Wirkung auf die Skelettmuskulatur [125]. Auf der Grundlage der Arbeiten von Diel et al. sowie Isenmann et al. [125,124] wird in dieser Studie untersucht, ob die kombinierte Aufnahme von Eiweiß und Kohlenhydraten aus natürlichen Eiweißquellen direkt nach dem Training auch bei postF und älteren Personen zu einer Steigerung der Trainingsadaption, vor allem der Muskelkraft, führen kann.

<u>Methode: Studie A:</u> Es wurden 58 Frauen zwischen 50 und 65 Jahren rekrutiert. Einschlusskriterien waren der postmenopausale Status, wobei die letzte Menstruation mindestens zwei Jahre zurückliegen musste. Ausschlusskriterien waren hormonelle Erkrankungen, Stoffwechselkrankheiten, behandlungsbedürftige Herzrhythmusstörungen und einschränkende neurologische, muskuläre, degenerative oder gastrointestinale Erkrankungen. Unausgewogene Ernährung z. B. vegane

Ernährung, Rauchen und Hormonsubstitutionen jeglicher Art waren ausgeschlossen. Alle Frauen hatten einen niedrigen bis mäßigen Fitnessstatus. Es wurden Blutentnahmen, die Erhebung der anthropometrischen Daten (Gewicht, Größe, Bauchumfang) und eine BIA Messung (BodyExplorer, Kommunikation & Service GmbH, Berliner Chaussee 74, 15234 Frankfurt, Oder) durchgeführt. Zur Bestimmung der Ausdauerleistungsfähigkeit wurde ein Laktatstufentest auf einem Laufband (Woodway PPS55med, Woodway GmbH, Steinackerstr. 20, 79576 Weil am Rhein) durchgeführt. Die Handgriffkraft, Beinkraft und Brustkraft wurden gemessen. Danach folgte die Randomisierung mittels Computerprogramms (RITA Version 1.51).

Intervention Studie A: Zur Eingewöhnung fand das Ausdauertraining (Walking) drei Wochen lang mit einer Geschwindigkeit von die 60 % der 4 mmol-Laktatschwelle statt. In den folgenden 9 Wochen wurde das Training auf 75% km/h der 4 mmol-Laktatschwelle gesteigert. Die Gehgeschwindigkeit und die Herzfrequenz wurden mit der Sportuhr Polar Ignite überwacht. Das Online-Krafttraining wurde zweimal pro Woche über Cisco Webex Meetings (Cisco Systems GmbH) angeboten. Alle Teilnehmer mussten 80 % des Ausdauertrainings und 100 % des Krafttrainings absolvieren. Das Krafttraining bestand aus Körpergewichtsübungen wie Kniebeugen, Crunches, Dips und Planks für alle großen Muskelgruppen, wie M. quadriceps femoris, M. ischiocrurales, Mm. pectorales, M. triceps brachii, M. biceps brachii, Mm. glutei und die Rumpfmuskulatur (Abbildung 5). Während der 12 Wochen der Intervention durften die Frauen keine andere Sportart betreiben. Nach jeder Trainingseinheit erhielten die Frauen eine Protein/Kohlenhydrat Supplementation (Tabelle 3).

Tabelle 3: Nahrungsintervention Studie A und B

Studie A	**100 g Sauermilchkäse und 76 g Toastbrot**
Proteine (g)	36,1
Kohlenhydrate (g)	35,3
Fett (g)	3,5
kcal	321
Studie B	**100 g Sauermilchkäse and 76 g Toastbrot and 250 ml Buttermilch**
Proteine (g)	44,6
Kohlen-hydrate (g)	4,8
Fett (g)	5
kcal	416

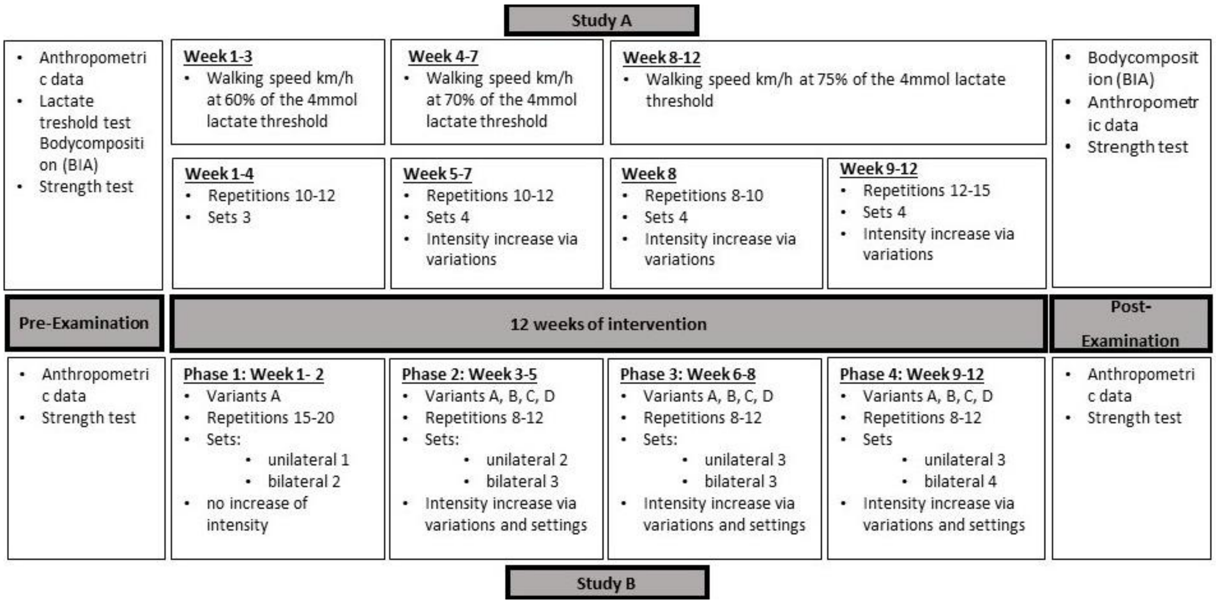

Abbildung 5: Originalabbildung: Trainingsprotokoll Studie A und Studie B

<u>Methode Studie B</u>: Es wurden 35 TeilnehmerInnen in die Randomisierung einbezogen. Alle TeilnehmerInnen absolvierten ein Schlingentraining in Anlehnung an Gaedtke. Einschlusskriterien waren ein Alter von über 60 Jahren und eine sportliche Aktivität von mindestens einem Jahr. Ausschlusskriterien waren eine akute Erkrankung des Bewegungsapparates, kardiovaskuläre Erkrankungen und Erfahrungen mit Schlingentraining. Die Maximalkraft für Brust- und Beinkraft wurde über das Wiederholungsmaximum nach Rühl ermittelt. Für die ventrale, dorsale und laterale Rumpfmuskulatur wurde zusätzlich der Swiss Olympic Rumpftest nach Tschopp durchgeführt.

<u>Intervention Studie B:</u> Das Training fand dreimal pro Woche statt und dauerte 30 Minuten. Die Interventions- und die Kontrollgruppe absolvierten das Training gemeinsam. Das Training wurde in vier Trainingsphasen von je zwei Wochen aufgeteilt (Abbildung 5). Jede Trainingseinheit umfasste sieben Übungen mit 90 Sekunden Pause zwischen jeder Übung. Die Reihenfolge der Übungen wurde so gewählt, dass eine Muskelgruppe nicht zweimal hintereinander beansprucht wurde. Die Anzahl der Wiederholungen wurde erhöht, nachdem eine Versuchsperson bei einer Übung im letzten Satz über zwei Trainingseinheiten zwei Wiederholungen mehr erreicht hatte (progressive Überlastung). Dadurch wurde eine Progression des Trainings gewährleistet, das mit acht Wiederholungen begann und mit zwölf Wiederholungen endete. Nach jeder Trainingseinheit erhielten die Teilnehmer eine Protein-Kohlenhydrat Supplementation (Tabelle 3).

Ergebnisse: Studie A: 51 postmenopausale Frauen (57.3 ± 3.0 Jahre) beendeten die Studie (Tabelle 4).

Tabelle 4: Anthropometrische Daten Studie A (MW und SD)
IG: Interventionsgruppe, CG: Kontrollgruppe

	Gesamt	**IG**	**CG**
Studie A	N = 51	N = 24	N = 28
Alter (Jahre)	57,3 ± 3.0	57,9 ± 3.3	56,8 ± 2.8
Größe (cm)	167 ± 7.3	169,8 ± 6.9	164,6 ± 6.7
Gewicht (kg)	69,7 ± 12.7	70,8 ± 15.2	68,8 ± 10.3
BMI	25,1 ± 4.4	24,5 ± 4.7	25,5 ± 4.2

Tabelle 5 zeigt die Ergebnisse der Kraftwerte und die Veränderung der Körperzusammensetzung. Die einzelnen Kraftparameter konnten zum allgemeinen Kraftwert (General Strength Score) mittels PCA (Hauptkomponentenanalyse) und LME zusammengefasst werden. Wie in Abbildung 6 dargestellt konnte ein signifikanter Trainingseffekt (+0,65, p ≤ 0,001), nachgewiesen werden, die Supplementation zeigte keine signifikante Steigerung (ca. 0, p = ca. 0,85), auch wenn Tendenzen in der Handgriffkraft zu erkennen waren.

Tabelle 5: Kraftparameter und Körperzusammensetzung (MW und SD)
T0: vor der Intervention, T1: nach der Intervention, IG: Interventionsgruppe, CG: Kontrollgruppe

N = 51	**IG**		**CG**	
	T0	**T1**	**T0**	**T1**
Kraft				
Beine (kg)	89,9 ± 20,9	95,9 ± 24,2	91,4 ± 26,4	105,0 ± 25,9
Brust (kg)	28,0 ± 8,2	31,9 ± 8,4	25,5 ± 5,6	27,7 ± 5,7
Griffkraft rechts (kg)	28,9 ± 4,7	31,3 ± 4,0	27,8 ± 4,2	29,0 ± 3,9
Griffkraft links (kg)	27,9 ± 4,5	29,1 ± 3,9	26,8 ± 4,5	27,5 ± 4,3
Griffkraft gesamt (kg)	51,1 ± 18,9	54,2 ± 18,9	53,5 ± 9,4	56,5 ± 7,6
Körperzusam-mensetzung				
Gewicht	70,8 ± 15,2	70,5 ± 15,5	68,8 ± 10,5	68,1 ± 10,1
Muskelmasse	19,1 ± 2,4	19,3 ± 2,5	18,8 ± 1,8	19,2 ± 2,0
Fettmasse	25,6 ± 11,0	25,2 ± 11,1	24,4 ± 7,7	23,4 ± 7,1

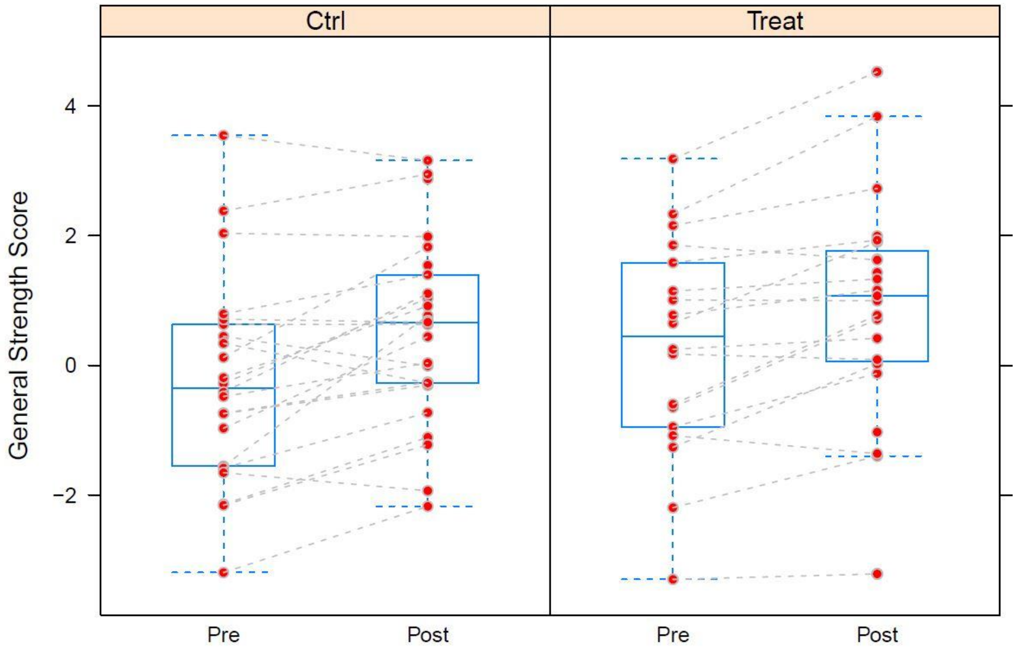

Abbildung 6: Originalabbildung: Box-Plots des allgemeinen Kraft-Scores (GS):

Anmerkung: berechnet aus den Kraftdaten der Studie A, gruppiert nach Supplementierung (Ctrl: Kontrollgruppe; Treat: Behandlungsgruppe). Pre: Messung vor der Trainingsintervention; Post:Messungen nach der Trainingsintervention. GS entspricht der 1. Hauptkomponente, die aus den Kraftdaten extrahiert wurde. Siehe Text für eine detaillierte Erläuterung des Scores. Die Box-Plots zeigen Minima, 1. Quartile, Mediane, zweite Quartile bzw. Maxima an. Maxima oder Minima, die über den Median ± das 1,5-fache des jeweiligen Interquartilsbereichs hinausgehen ("Ausreißer"), befinden sich außerhalb der Whisker. Gestrichelte Linien entsprechen wiederholten Messungen bei denselben Probanden.

<u>Ergebnisse Studie B</u>: 31 TeilnehmerInnen (6 Männer, 25 Frauen) (65.9 ± 4.9 Jahre) konnten die Studie abschließen (Tabelle 6).

Tabelle 6: Anthropometrische Daten Studie B (MW und SD dargestellt)

	Gesamt	**IG**	**CG**
Studie B	N = 31	N = 15	N = 16
Alter (Jahre)	65,9 ± 4,9	67,7 ± 5,9	64,2 ± 3,2
Größe (cm)	166,1 ± 8,5	165,3 ± 9,2	166,9 ± 7,9
Gewicht (kg)	85,4 ± 15,6	87,3 ± 14,9	83,6 ± 15,5
BMI	30,9 ± 5,1	31,8 ± 4,1	30,0 ± 5,7

Mittels PCA und LME wurde hier ein Kraftwert für den Rumpf (TS) und ein Kraftwert für die Extremitäten (LS) ermittelt. Die Rumpfkraft veränderte sich signifikant über die 12 Wochen Interventionszeit (+2.305, $p \leq 0.001$). Die Nahrungsergänzung hatte einen zusätzlichen und signifikant positiven Effekt auf die TS. LS stieg nach der Trainingsintervention signifikant an (+0,753, $p < 0,05$). Adipöse Probanden wiesen niedrigere Ausgangswerte auf (-1,683, p ≤ 0,05) und reagierten signifikant schwächer auf die Trainingsintervention (-1,513, p ≤ 0,01).

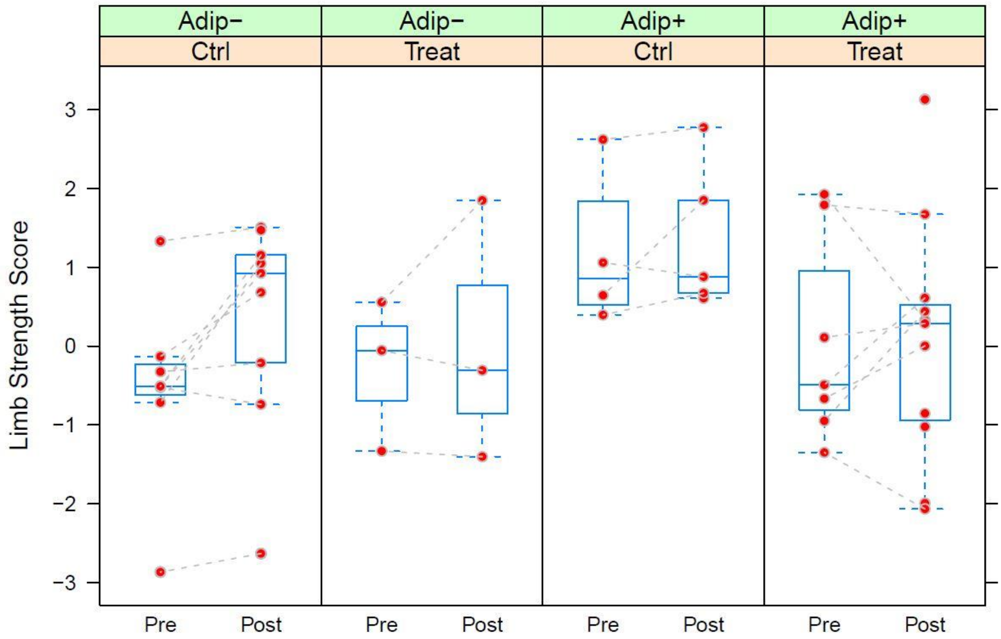

Abbildung 7: Originalabbildung: Box-Plots des aus den Kraftdaten der Studie B

Anmerkung: berechneten Limb Strength Score(LS) gruppiert nach Supplementierung (Ctrl: Kontrollgruppe; Treat: Behandlungsgruppe) innerhalb des Adipositas-Status (Adip-: BMI <30, Adip+: BMI >= 30). Pre: Messung vor der Trainingsintervention; Post: Messungen nach der Trainingsintervention. LS entspricht der 2. Hauptkomponente, die aus den Kraftdaten extrahiert wurde. Siehe Text für eine ausführliche Erläuterung des Scores.

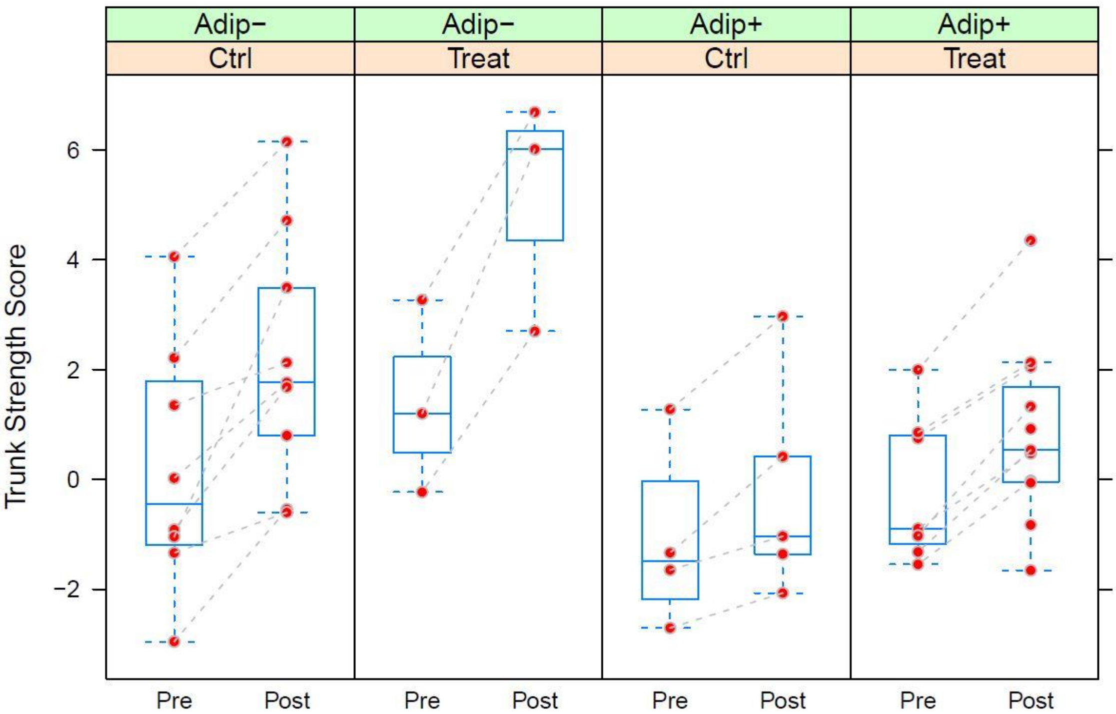

Abbildung 8: Originalabbildung: Box-Plots des aus den Kraftdaten der Studie B

Anmerkung: berechneten Trunk Strength Score(TS) gruppiert nach Supplementierung (Ctrl: Kontrollgruppe; Treat: Behandlungsgruppe) innerhalb des Adipositas-Status (Adip-: BMI < 30, Adip+: BMI >= 30). Pre: Messung vor der Trainingsintervention; Post: Messungen nach der Trainingsintervention. TS entspricht der 1. Hauptkomponente, die aus den Kraftdaten extrahiert wurde.

Diskussion: Beide Studien zeigten eine positive Wirkung des Trainings; das Schlingentraining steigerte die Kraft der Gliedmaßen und insbesondere des Rumpfes bei älteren Männern und Frauen. Verschiedene Studien zeigten einen positiven Effekt von Schlingentraining auf die Muskelmasse im Allgemeinen und die Rumpfmuskulatur im Besonderen [138,21,139]. Die Rumpfmuskelkraft wurde bei der IG nach der Supplementation stärker gefördert als bei der CG. Bei der Kraft der Gliedmaßen konnte dieser Effekt nicht nachgewiesen werden. Allerdings war das Training in der IG signifikant effektiver. Schlingentraining wird häufig zur Behandlung von Schmerzen im unteren Rückenbereich eingesetzt, die oftmals durch ein Defizit in der Rumpfmuskulatur ausgelöst werden. Eine Protein/Kohlenhydrat-Supplementierung verstärkte diese positiven Effekte, eventuell aufgrund der proregenerativen Effekte, die Isenmann et al. beschrieben haben [124]. Die älteren Teilnehmer beanspruchen ihre Bein- und Brustmuskeln im Alltag regelmäßig, so dass die proregenerativen Effekte keine große Wirkung zeigen konnten. Da jedoch im Alter die Rumpfmuskulatur abnimmt, ist ein Schlingentraining mit dem Schwerpunkt Rumpfstabilisierung, eine große Herausforderung und fordert diese Muskeln. Das Training wurde dreimal pro Woche angeboten. Daher kann es zu proregenerativen Effekten kommen, wie z. B. einem Anstieg der Insulin-Serumkonzentration, einem Rückgang der proinflammatorischen Marker und einem Anstieg der antiinflammatorischen Marker. Isenmann et al. zeigten diese Effekte bei jungen Männern nach einer ähnlichen Protein-/Kohlenhydrat-Supplementierung über die Nahrung unmittelbar nach dem Training [124]. Die positive proregenerative Wirkung einer Protein-/Kohlenhydrat-Supplementierung nach dem Training wurde auch von anderen Autoren nachgewiesen [136,140]. Der signifikante Trainingseffekt war bei Teilnehmern mit einem höheren BMI (>30) weniger ausgeprägt als bei Teilnehmern mit einem niedrigeren BMI. Eine mögliche Erklärung könnte sein, dass bei höherem Körpergewicht die Übungen nicht so gut oder nur in einfacheren Variationen ausgeführt werden konnten, was einen geringeren Trainingseffekt verursacht haben könnte. Zusammenfassend lässt sich sagen, dass bei den Senioren durch das Training ein signifikanter Kraftzuwachs erzielt wurde, was insbesondere im Hinblick auf das Risiko einer Sarkopenie sehr positiv ist. Die Nahrungsergänzung in Form einer Abendmahlzeit steigerte die Rumpfkraft noch deutlicher, was ein wichtiger Aspekt im Hinblick auf die Gebrechlichkeit im Alter ist.

Die Kombination von Ausdauer- und Krafttraining steigerte bei postF die Kraft und die Frauen fühlten sich leistungsfähiger. Auswirkungen auf die Ganzkörperkraft wurde nachgewiesen. Die Auswirkungen auf die Griffkraft sind für postF wichtig, da viele von ihnen eine geringe Knochen- und Muskelmasse haben, was mit einer geringen Griffkraft einhergeht. Darüber hinaus wird eine geringe Handgriffstärke mit einer geringen Lebensqualität in Verbindung gebracht [141]. Mit Hilfe der Hauptkomponentenanalyse zeigten wir und andere Autoren , dass die Handgriffstärke als Indikator für die Gesamtkörperstärke verwendet werden kann [142]. Diese Ergebnisse stehen im Einklang mit der Zunahme und der Rolle der Handgriffstärke. Somit würde die Zunahme der Handgriffkraft die Zunahme des subjektiven Fitnesszustands der Teilnehmer erklären.

In Studie B kam es zu einer signifikanten Abnahme des Körpergewichts; in Studie A konnten wir dies nicht nachweisen. Allerdings waren die Teilnehmer in Studie A mit einem BMI von 25,1 normal bis leicht übergewichtig im Vergleich zu den Teilnehmern in Studie B (BMI 30,9). Zudem wurde in Studie B dreimal pro Woche ein Krafttraining durchgeführt, während in Studie A zweimal pro Woche ein moderates und fettstoffwechselorientiertes Ausdauertraining und nur einmal pro Woche ein Krafttraining durchgeführt wurde. So hatte das Ausdauertraining einen effektiven Effekt auf die Fettmasse, während das Krafttraining einen schnelleren Effekt auf das Körpergewicht hatte [143].

Der Ernährungs- und Proteinstatus wurde in keiner der beiden Studien vor und während des Trainings erfasst, was für die Identifizierung möglicher Defizite in der Versorgung oder einer Überversorgung mit Nahrungsprotein hilfreich gewesen wäre, zumal die Wirkung der Protein-/Kohlenhydratsupplementierung bei älteren Teilnehmern so ausgeprägt war. In Studie B wurde eine Protein-/Kohlenhydratergänzung in Form einer gemeinsamen Mahlzeit am Abend nach dem Training angeboten. In Studie A war dies nicht gegeben, da aufgrund der COVID-19-Pandemie nach dem Training keine gemeinsame Mahlzeit möglich war. In Studie B wurde die Körperzusammensetzung nicht bestimmt, so dass zwar Rückschlüsse auf die Veränderung des Körpergewichts, nicht aber auf die genaue Körperzusammensetzung gezogen werden konnten. Diese Parameter wären hilfreich gewesen, um neue Erkenntnisse zum Einfluss von Training und Protein-/Kohlenhydratzufuhr auf die Muskel- und Fettmasse zu erhalten. Da das Körpergewicht der Probanden in Studie B signifikant höher war (85,4 ± 15,6 kg) als das der Probanden in Studie A (69,7 ± 12,7 kg), wäre die genaue Körperzusammensetzung ein interessanter Parameter gewesen, um die Ausgangsmuskel- und -fettmasse zu vergleichen.

Konklusion: Die Ergebnisse deuten darauf hin, dass eine Kombination aus Training und einer Protein-/Kohlenhydrat-Supplementierung über die Nahrung direkt nach dem Training eine geeignete Strategie sein könnte, um dem altersbedingten Verlust der Rumpfkraft bei Senioren entgegenzuwirken. Die Kombination aus Kraft- und Ausdauertraining bei postmenopausalen Frauen und Schlingentraining bei älteren Personen führte zu einer Verbesserung der Kraft. Wir wiesen den Einfluss einer Protein-/Kohlenhydratsupplementierung nur in Bezug auf bestimmte Parameter nach, was jedoch auf methodische Einschränkungen und die COVID-19-Pandemie zurückzuführen sein könnte.

4.3 Publikation 3: "Serum Stable Calcium Isotopes ($^{44}Ca/^{42}Ca$) indicate beneficial Effects of moderate Training on Bone Metabolism in postmenopausal Women." Under review

Einleitung: Im Jahr 2021 litten etwa 18 % der Weltbevölkerung an Osteoporose [99]. Die Belastung durch die Krankheit ist enorm, und die Prävalenz der Osteoporose steigt weiter an [144]. Frauen weisen durchgängig eine höhere Prävalenz und Inzidenzen auf [145,99]. Dies ist auf den mit der Menopause einhergehenden Östrogenmangel zurückzuführen [98]. Studien zur Pathogenese deuten auf einen überwiegenden Verlust an Knochenmasse während der Perimenopause [146] und innerhalb weniger Jahre nach Beginn der Menopause hin [147,148]. Zusätzlich zur Mikronährstoffzufuhr und zum Verzicht auf Alkohol und Nikotin ist regelmäßige Bewegung für die Knochengesundheit von Vorteil [98,100,149]. Die prospektive Bewertung der für das metabolische Gleichgewicht des Knochens vorteilhaften Bewegungsmengen (BMB) erweist sich als schwierig. Insbesondere die konventionelle Messung der Knochenmineraldichte (BMD) mittels Dual-Energy-Röntgenabsorptiometrie (DXA) weißt erhebliche methodische Probleme auf [112]. Zum einen reagiert dieser Proxy nur langsam. Zum anderen ist die wiederholte Strahlenbelastung gesunder Personen ethisch problematisch. Am wichtigsten ist jedoch, dass die DXA lediglich an bestimmten Stellen des Skeletts durchgeführt wird. Eisenhauer et al. schlagen eine $^{44}Ca/^{42}Ca$-Analyse in Blut und Urin zur Beurteilung der BMB vor [112]. Die Methode wießt eine ausgezeichnete diagnostische Aussagekraft auf. Sie nutzt die physiologische Ca-Isotopen Fraktionierung während der Knochenmineralisierung. Insbesondere geben die $^{44}Ca/^{42}Ca$-Verhältnisse den Brutto-Knochenstoffwechsel wieder. Vorteilhaft ist auch die fehlende Strahlenbelastung, was es für Längsschnittstudien unkritisch macht. Das Ziel der vorliegenden Studie war die Bewertung der potenziell positiven Auswirkungen eines moderaten Krafttrainings- und Ausdauertrainings auf die Knochengesundheit bei postmenopausalen Frauen. Die $\delta^{44}/^{42}Ca$-Serumwerte dienten als Indikator für den Knochenstoffwechsel.

Methode: 51 postF nahmen an einer 12-wöchigen Trainingsintervention (Ausdauertraining (Gehen, zweimal/ Woche) und Körpergewichtstraining (einmal/ Woche) sowie einer Protein/ Kohlenhydrat Supplementation teil. Erhoben wurden das Verhältnis der stabilen Ca-Isotope im Serum ($^{44}Ca/^{42}Ca$ durch ICP-MC-IRMS), die Bein- und Brustkraft, die Handgriffkraft, die tägliche Schrittäquivalente und Körperzusammensetzung. Alle Messungen wurden vor und nach dem Interventionsintervall durchgeführt.

Ergebnisse: 26 Frauen (57,0 ± 2,7 Jahre) wurden innerhalb der Subgruppe untersucht. Der Kraftwert, mittels PCA ermittelt aus den Daten der drei Krafttestungen konnte signifikant verbessert werden. Die Körperzusammensetzung hingegen veränderte sich nicht signifikant. Die Serum $\delta^{44}/^{42}Ca$-Werte der Teilnehmerinnen stiegen um 0,057 ‰ ($p < 0{,}001$, LME) (Abbildung 9).

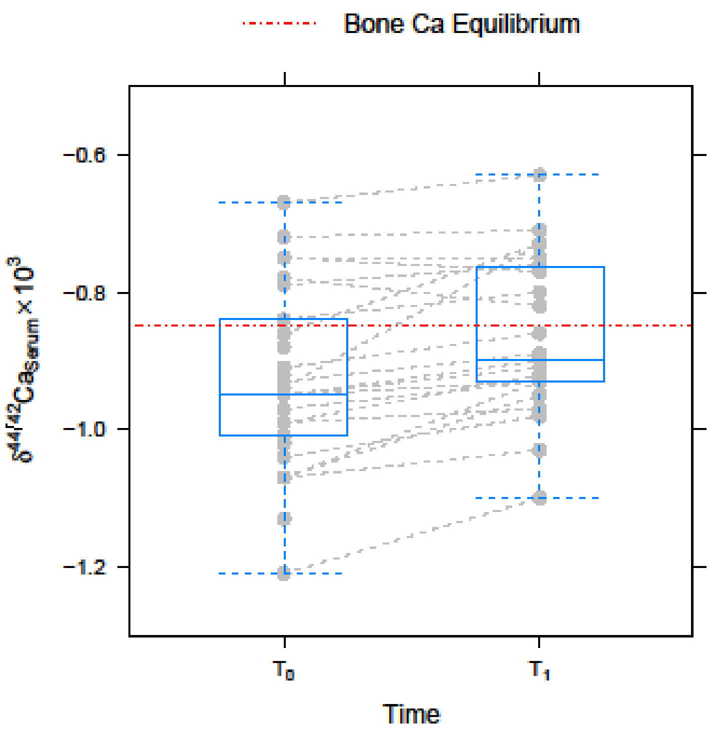

Abbildung 9: Originalabbildung: Darstellung der Serum-δ44/42Ca-Werte
Anmerkung: vor (T0) und nach (T1) der 12-wöchigen Intervention. Die rote Linie stellt das Gleichgewicht des Knochenmetabolismus dar.

Einzelne Abschnitte und Veränderungen korrelierten signifikant ($\rho = -0{,}52$, $p < 0{,}05$, LME-Likelihood Statistik). Mittels LME konnte ein deutlich signifikanter Trainingseffekt auf den Ca-Serum Spiegel nachgewiesen werden. Es konnten keine signifikanten Auswirkungen irgendeiner Kovariable (Alter, Körperkraft, Körperzusammensetzung, gelaufenen Schritte) festgestellt werden.

Diskussion: Der durchschnittliche $\delta^{44}/^{42}$Ca-Wert betrug vor dem Training -0,927 ‰. Dies liegt deutlich unter dem metabolischen Gleichgewichtsäquivalent von -0,85 ‰ Der Anstieg um 0,057 ‰ deutet nicht auf eine vollständige Abfederung des Katabolismus hin. Sie stellt jedoch zweifellos eine wesentliche Verbesserung dar. Außerdem war das moderate Trainingsprogramm für die Probanden im Allgemeinen attraktiv. Die Compliance war ausgezeichnet, und es gab nur wenige Abbrüche. Das Design entsprach eher Freizeitsport als einem knochenspezifischen Training. Es ist daher bemerkenswert, dass die Intervention trotzdem hoch signifikante Knochenstoffwechsel Verbesserungen bewirkt. Gehen erhöht die BMD vor allem im Oberschenkelhals, aber kombinierte Belastungen wirken eher auf die Lendenwirbelsäule. Kombinierte Belastungen stimulieren also den Knochenstoffwechsel auf systemischer Ebene [111,132,106]. Dies stimmt mit unseren Ergebnissen überein. Die Beziehung zwischen dem Körpergewicht und BMD ist nicht eindeutig [150]. Es wurde sogar ein positiver Zusammenhang vermutet. Aufgrund der erhöhten mechanischen Stimulation scheint dies möglich zu sein. Adipositas kann aber auch zu einer negativen BMB aufgrund der Stimulation von Osteoklasten führen [151]. Sherk et al. unterstützen diese Ansicht [147]. Seifert et al. konnten jedoch keine Korrelation zwischen BMI und Knochenverlust während des Übergangs in die Wechseljahre feststellen [146]. Auch in der vorliegenden Studie wurde keine signifikanten Auswirkungen der Körperzusammensetzung auf ^{44}Ca/^{42}Ca festgestellt. Außerdem wies keine der Personen (n=2, BMI > 30) auffällige Werte auf. Die Bedeutung von Bewegung zur Prävention von Osteoporose ist grundsätzlich unbestritten [152]. Es wird jedoch intensiv nach optimalen Bewegungsempfehlungen gesucht. Obwohl aus vielen anderen Gründen vorzuziehen, erscheint gesundheitsorientiertes Gehen allein nicht zielführend [152]. Dies spiegelt sich in den vorliegenden Ergebnissen wider, dass Schrittäquivalente keinen Einfluss auf den eher systemischen Biomarker $^{44}Ca/^{42}Ca$ haben. Der F-Score, d. h. die systematisch kombinierte Kraftleistung, kommt der funktionellen Fitness wahrscheinlich sehr nahe. Sein hochsignifikanter Anstieg beweist die Wirksamkeit des Trainings. Der F-Score und $^{44}Ca/^{42}Ca$-Verhältnisse sind voneinander unabhängig, ebenso die entsprechenden Veränderungen der beiden Maße. Dies steht im Widerspruch zu den Ergebnissen von Sherk et al. [147], die eine Korrelation zwischen BMD- und Kraftdaten feststellten. Die Autoren verwendeten lokalisierte BMD-Messungen, und wie bereits betont, spiegeln die $^{44}Ca/^{42}Ca$-Verhältnisse vorteilhafterweise eher die systemische BMB wider.

Konklusion: In Übereinstimmung mit anderen Studien [106] kommen wir zu dem Schluss, dass einige wenige aufwändige und individuell angepasste Trainingseinheiten pro Woche ausreichend sind. Zumindest in Bezug auf die hier untersuchten Intervalle (12 W) scheint das Training selbst die Effekte spezifischerer Kovariaten zu übertreffen. Bloßes Körpergewichtstraining scheint ausreichend zu sein.

4.4 Publikation 4: “Resistance training alters body composition in middle-aged women depending on menopause - A 20-week control trial. 2023, BMC Women´s Health, 23(1), 526; DOI: 10.1186/s12905-023-02671-y

Einleitung: Mit fortschreitendem Alter reduziert sich ohne Gegenmaßnahmen die Muskelmasse (MM). Es hat sich gezeigt, dass die MM bei Männern und Frauen nach dem 30. Lebensjahr um 3 bis 8 % und nach dem 50. Lebensjahr um 5 bis 10 % pro Jahrzehnt abnimmt [62]. Bei Frauen wird dieser Prozess durch die Menopause verstärkt. PostF mit verminderter Muskelmasse haben ein 2,1-fach höheres Sturzrisiko und ein 2,7-fach höheres Risiko für Knochenbrüche als Frauen mit erhaltener Muskelmasse [49]. Da es sich bei der Skelettmuskulatur um ein stoffwechselaktives Gewebe handelt, können auch altersbedingte Stoffwechselstörungen wie Diabetes mit der Abnahme der Muskelmasse in Verbindung gebracht werden [62]. Gerätegestütztes Widerstandstraining (RT) wirkt dem alters- und wechseljahresbedingten Verlust an MM und Kraft bei Frauen entgegen [63]. Daher ist es nicht verwunderlich, dass die WHO empfiehlt, dass alle Erwachsenen mindestens zweimal pro Woche mit mäßiger oder höherer Intensität muskelstärkende Aktivitäten durchführen sollten, die alle wichtigen Muskelgruppen einbeziehen, um der Gesundheit zu dienen [153]. Das American College of Sports Medicine (ACSM) ist in seinen Richtlinien für RT von 2009 spezifischer [60]. Darin heißt es, dass untrainierte Personen zwei bis dreimal pro Woche mit freien Gewichten und Maschinen (Ein- und Mehrgelenksübungen) ihren gesamten Körper mit ein bis drei Sätzen pro Übung, 8-12 Wiederholungen (60-70 % 1-RM für Kraft; 70-85 % 1-RM für Hypertrophie) und ein bis drei Minuten Pause (je nach Übungsauswahl) trainieren sollten. Aktuelle Forschungsergebnisse deuten darauf hin, dass nur fünf bis sechs Sätze pro Muskelgruppe und Woche für Anfänger ausreichend sind, um einen Effekt zu erzielen [63,154]. Die derzeitigen Empfehlungen beruhen jedoch auf Daten von Männern. Nur 2 % bis 14 % der Artikel in drei großen Sport- und Fitnessmagazinen enthielten ausschließlich Frauen als Teilnehmerinnen [155], so dass es möglicherweise einen geschlechtsspezifischen Unterschied bei den Trainingsempfehlungen geben könnte. Folglich sind mehr qualitativ hochwertige Forschungsergebnisse zu fördern, um geschlechts- und altersspezifische Empfehlungen für wirksame RT-Programme während des Alterns zu geben.

Methode: 41 gesunde Frauen (40-60 Jahre) nahmen an dieser Studie teil (T0-T1: Kontrollphase; T1-T2: RT zweimal wöchentlich). Die Probandinnen wurden nach dem Zufallsprinzip einer RT-Gruppe mit niedriger (50% 1-RM) oder mäßiger Intensität (75% 1-RM) zugeteilt und entsprechend ihrem Hormonprofil in Prä- und Postmenopause eingeteilt. Fettfreie Masse (FFM), MM, Fettmasse (FM), Muskeldicke (Vastus lateralis [VL], Rectus femoris [RF], Triceps brachii [TB]), Griffkraft, 1-RM-Hocke und Bankdrücken wurden vor und nach jeder Phase bewertet.

Ergebnisse: Während der Intervention kam es zu keinen Verletzungen. Signifikante Steigerungen der 1-RM wurden in allen Gruppen beobachtet. Für die dynamischen Kraftparameter wurde kein Interaktionseffekt beobachtet. Bei präFFrauen nahmen FFM, MM und RF-Muskeldicke signifikant zu, während die VL nur einen Trend zeigte. Diese Effekte waren bei postF unabhängig von der RT-Intensität nicht vorhanden.

Diskussion: RT mit freien Gewichten ist für Frauen mittleren Alters zur Steigerung der 1-RM sicher und wirksam. Um Hypertrophie und/oder Veränderungen in der Körperzusammensetzung zu erreichen, sind für Frauen nach der Menopause wahrscheinlich größere Trainingsvolumina (>sechs bis acht Sätze/Muskel und Woche) erforderlich. Im Allgemeinen fehlt es an Studien zur RT bei Frauen mittleren Alters, die nur mit freien Gewichten trainieren. Übungen mit freien Gewichten, wie z. B. Kniebeugen und Bankdrücken sind möglicherweise ideal, um die Kraft mit einem höheren Grad an Spezifität im Sinne der ADL´s zu steigern als bei einem maschinellen Training [106]. Derzeit gibt es keine Studien, die die Auswirkungen von RT mit freien

Gewichten, mit denen von maschinellem Training bei älteren Frauen vergleichen. In der vorliegenden Studie konnte jedoch gezeigt werden, dass RT mit freien Gewichten bei Frauen mittleren Alters sicher und effektiv eingesetzt werden kann.

Die Kraftzuwächse in der Studie sind vergleichbar mit den in früheren Untersuchungen berichteten Effekten [156,157]. Im Vergleich dazu zeigten Karaaslan et al. einen stärkeren Effekt bei vier Trainingseinheiten/Woche über 12 Wochen mit maschinenunterstütztem Training [158]. Ähnlich wie bei männlichen Teilnehmern zeigen die Studien an Frauen mittleren Alters eine vergleichbare Dosis-Wirkungs-Beziehung bei den Anpassungsprozessen der Muskelkraft [159]. Interessanterweise wurden in dieser Studie keine Unterschiede zwischen prä- und postF festgestellt. Die Veränderung der endokrinen Homöostase hat wahrscheinlich keinen signifikanten Einfluss auf die Kraftkapazität bei untrainierten gesunden Frauen mittleren Alters. Im Vergleich zur dynamischen Kraft gab es bei der isometrischen Griffkraft nach der Trainingsintervention in keiner Gruppe einen Anstieg. Überraschenderweise verbesserte sich die Griffkraft während der Interventionsphase nicht, obwohl die meisten Übungen, die durchgeführt wurden, einen starken Griff erfordern, z. B. die seitliche Beugung, das Langhantelrudern und der Latzug. Ähnlich wie bei den hier vorgestellten Daten hatte das RT an Maschinen über 12 Wochen und drei Trainingseinheiten pro Woche keine Auswirkungen auf die Griffkraft [160]. Interessanterweise ist die Griffkraft ein wichtiger Prädiktor für den Muskelstatus [161]und wird regelmäßig zur Abschätzung des Risikos der Gesamtmortalität bei älteren Menschen verwendet [162]. Wenn jedoch die Gesamtkörperkraft durch RT mit freien Gewichten verbessert werden kann, nicht aber die Griffkraft, muss die Beziehung zwischen der Griffkraft, dem Muskelstatus und somit der Sterblichkeit möglicherweise erneut untersucht werden.

FM nahm nur in der PräF MI-RT-Gruppe signifikant ab. Die Ergebnisse der beiden postmenopausalen Gruppen bestätigen nicht die Beobachtungen aus früheren Studien. Sowohl Kang et al. [160] als auch Delshad et al. [163] beobachteten eine signifikante Abnahme des Körperfetts nach 12 Wochen RT. Ähnlich wie bei den Auswirkungen auf die MM spielen auch bei der FM die Trainingshäufigkeit und das Trainingsvolumen eine entscheidende Rolle. Diese Annahme kann durch die Ergebnisse von Rodrigues et al. gestützt werden, wo in einer 12-wöchigen Interventionsstudie mit zwei Trainingseinheiten pro Woche, einschließlich RT und Ausdauerübungen, die FM nicht abnahm [164]. Die Intensität des Trainings wurde durch eine subjektive Anstrengungswahrnehmungsskala kontrolliert, wobei die Intensität zwischen 13 und 15 gehalten wurde [164]. Daher waren sowohl die Intensität als auch die Häufigkeit der Krafttrainings vermutlich zu gering, um den Fettstoffwechsel zu aktivieren.

Konklusion: RT mit freien Gewichten ist für Frauen mittleren Alters zur Steigerung der 1-RM sicher und wirksam. Um Hypertrophie und/oder Veränderungen in der Körperzusammensetzung zu erreichen, sind für postF wahrscheinlich größere Trainingsvolumina (>sechs bis acht Sätze/Muskel und Woche) erforderlich.

4.5 Publikation 5: "Effects of endurance training on thyroid response in pre- and postmenopausal women." Under review

Einleitung: Altersbedingte Veränderungen der Schilddrüsenfunktion sind gut untersucht. Die Zahl der Schilddrüsenerkrankungen z.B. Krebs oder Hypothyreose steigt bei Frauen besonders in der peri- und postmenopausalen Lebensphase an [37,36]. Bedingt durch die enge Verknüpfung der Hormon-Achsen, den Alterungsprozess und die vielfältige Ausprägung der menopausalen Beschwerden ist eine genaue Diagnose häufig erschwert [36,37,165]. Ebenso konnten Einflüsse von körperlicher Aktivität auf die Schilddrüse festgestellt werden. Studien, die den Einfluss von (Ausdauer-)Training auf die Schilddrüsenfunktion bei postF untersucht haben, gibt es nicht [166–169]. Daher wird in dieser Pilotstudie zum einen die Schilddrüsenhormonausschüttung nach akutem Ausdauertraining bei präF und postF untersucht und zum anderen der Einfluss der Ausdauerintervention auf die Schilddrüsenfunktion bei postF erforscht.

Methode: 12 prä- und 12 postF wurden eingeschlossen. Bei allen Probandinnen wurden Größe, Gewicht und Körperzusammensetzung bestimmt. TSH, fT4 und fT3 wurden um 9:00 Uhr und 9:40 Uhr in Ruhe und nach einer akuten Ausdauerbelastung bestimmt. Um zyklusbedingte Einflüsse der präF auszuschließen, wurden die Untersuchungen in der Luthealphase des Menstruationszyklus durchgeführt. Hormonelle Verhütungsmethoden führten zum Ausschluss aus der Untersuchung. Es folgte für die postF eine sechswöchige Walking-Intervention. Während der Intervention führten die Probandinnen dreimal pro Woche für jeweils 45 Minuten ein Walking-Training bei 55 % - 70 % der HFmax durch. Nach der Interventionszeit wurden die Messungen wiederholt (Abbildung 10).

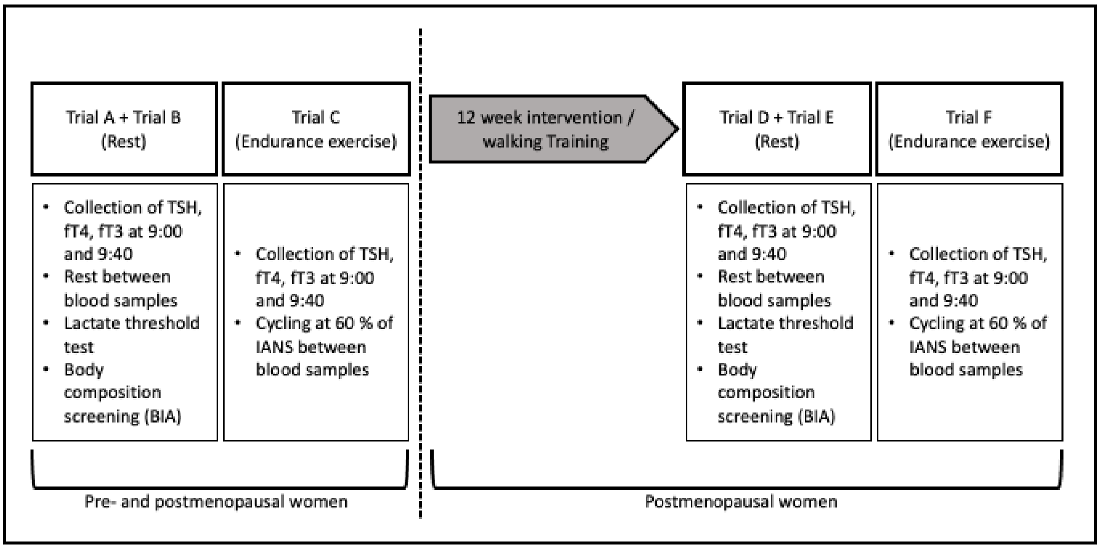

Abbildung 10: Originalabbildung: Zeitlicher Ablauf der Studie

Ergebnisse: Zu Beginn der Intervention war die MM der postF, um 3,13 kg bzw. 9,37% signifikant niedriger und die FM mit 8,99 kg bzw. 8,73% signifikant höher ($p<.05$) als bei den präF. Die FM nahm ab und die MM nahm während der Trainingsphase bei den postF zu ($p<.05$). Eine erhöhte TSH-Antwort wurde signifikant bei präF ($p=.028$) und nicht signifikant bei postF ($p=.135$) nach akuter Belastung festgestellt. Bei fT3 und fT4 gab es in beiden Gruppen keine Veränderungen. Nach der Intervention zeigten postF eine signifikante Verringerung der fT3-Reaktion ($p=.015$) und eine nicht signifikante Verringerung der TSH-Reaktion ($p=.432$).

Diskussion: Wie auch in anderen Untersuchungen unterschieden sich die präF im Hinblick auf die Fett-, Muskelmasse und das Körpergewicht signifikant voneinander [45,46,69,71]. Eine mögliche Ursache ist die reduzierte E2 Menge der postF [13,48,68]. Das Ausdauertraining wirkte sich positiv auf die Körperzusammensetzung der postF aus. Dies zeigten auch schon andere Autoren [58,59,67,89].

Gegenüber den präF reagierten die postF auf die akute Belastung mit einem TSH-Anstieg, auch wenn dieser nicht signifikant war. Ein Grund dafür könnte die kleine Stichprobe sein. Dennoch deuten die Daten darauf hin, dass die Frauen auf den akuten Trainingsreiz mit einer TSH- Freisetzung reagierten, um den höheren Bedarf an Schilddrüsenhormonen zu decken. Andere Autoren konnten diesen Effekt bereits nachweisen [167,170].

Dieser Anstieg des TSH konnte nach der Interventionsphase nicht mehr nachgewiesen werden, zudem war die fT3 Freisetzung ebenfalls signifikant geringer als vor dem Training. Über diese Ergebnisse besteht in der Literatur keine Einigkeit, ebenso fehlt

es an klaren Erläuterungen für die biologische Anpassung der Schilddrüse unter solchen Bedingungen [167,168,171,170,172].
Es scheint als hätte das Ausdauertraining bei den postF zu einer geringeren Ausschüttung von Schilddrüsenhormonen geführt. Dafür sprechen die geringere fT3 Freisetzung und der TSH-Abfall. Der Trainingsreiz führte bei den Frauen aber auch zu einer verbesserten Koordination und Fitness, was eine geringere Stoffwechselaktivität als vor der Intervention bedingte und die Belastung als leichter empfunden wurde. Allerdings zeigen tierexperimentelle Untersuchungen auch, dass Ausdauertraining zu einer gesteigerten Expression der Schilddrüsenhormonrezeptoren führt. Das würde erklären, dass niedrigere Konzentrationen der Schilddrüsenhormone gleiche bzw. verstärkte Effekte im Zielgewebe auslösen können [173,174].
Dennoch ist die untersuchte Stichprobe mit n=12 sehr gering und daher nur als erste Pilotstudie zu werten. Zudem sind alle Untersuchungen während der Corona-Pandemie durchgeführt wurden. Es mussten spontane Anpassungen der Methode erfolgen (Walkingintervention aber Belastungstest auf dem Fahrrad). Zudem entsprach der Alltag der Frauen durch Lockdown Situationen und Homeoffice Vorgaben nicht dem klassischen Alltag.
Konklusion: Diese Studie liefert den Beweis, dass sowohl prä- als auch postF mit einer Schilddrüsenstimulation auf ein akutes Ausdauertraining reagieren. Darüber hinaus liefert diese Studie erste Hinweise darauf, dass ein Ausdauertraining die Schilddrüsenreaktion nach akutem Ausdauerreiz bei postF reduzieren kann.

5. Gesamtresümee

Die Menopause und deren Folgen belastet die meisten Frauen sehr. Nicht nur dass diese das tatsächliche Ende der fortpflanzungsfähigen Phase im Leben einer Frau darstellt, sondern viele Frauen fühlen sich durch die menopausalen Symptome im Alltag eingeschränkt [175]. Neben Hitzewallungen, Abnahme der Muskelmasse und androgener Fettanlagerung gibt es aber auch versteckte Folgen der Menopause, wie beispielsweise das gesteigerte Risiko für kardiovaskulären Erkrankungen und das MetS [1,5,13,45,68,69,71]. Immer wieder wird, gerade bei Hitzewallungen und Stimmungsschwankungen die Hormonersatztherapie (HRT) empfohlen [1]. Da diese aber mit Risiken (z.B. Thromboserisiko, Brustkrebsrisiko) verbunden ist und viele Frauen auf die Verwendung von Hormonen verzichten wollen, suchen die Betroffenen nach Alternativen [176,177]. Körperliche Aktivität kann, wie in den vorliegenden Arbeiten dargestellt, den Umgang mit den Symptomen und die Gesunderhaltung positiv fördern [28,178] . Allerdings gibt es bisher zwar eine Vielzahl von Studien und Empfehlungen, aber viele Daten beruhen auf Untersuchungen an Männern oder jungen Frauen, so dass die hormonelle Situation nicht mit der der postF übereinstimmt [23,155]. Allgemeingültige Guidelines und damit Handlungsempfehlungen fehlen. Ergänzend dazu wird häufig nur ein Aspekt in den Untersuchungen berücksichtigt, sodass Frauen, die von mehreren Symptomen betroffen sind keine geeignete Empfehlung finden. Im Rahmen dieser kumulativen Dissertation wurde sich zunächst mit der Reaktion des Stoffwechsels auf eine akute Ausdauerbelastung auseinander gesetzt - hier zeigte sich eine völlig andere Stoffwechselantwort auf einen akuten Ausdauerreiz als bei präF. Basierend auf diesen Erkenntnissen wurde ein Training in Kombination mit einer Protein/Kohlenhydrat Supplementation und dessen Effekte auf die Körperzusammensetzung, die funktionelle Kraftfähigkeit und den Knochenstoffwechsel untersucht. Ebenso wurde die Wirkung von einem reinen Krafttraining mit freien Gewichten auf die Körperzusammensetzung und funktionelle Kraftfähigkeit hin überprüft. Da die Menopause häufig kombiniert ist mit Störungen der Schilddrüse, die Symptome nicht immer leicht zu differenzieren sind [36,37] und es keine Studien bei postF zur Schilddrüsenreaktion auf einen Ausdauerreiz hin gibt, wurde im Anschluss in einer Pilotstudie die Reaktion der Schilddrüse auf einen akuten und einen chronischen (12W) Ausdauerreiz untersucht. Im Folgenden werden nun die Forschungsfragen aufgegriffen und diskutiert.

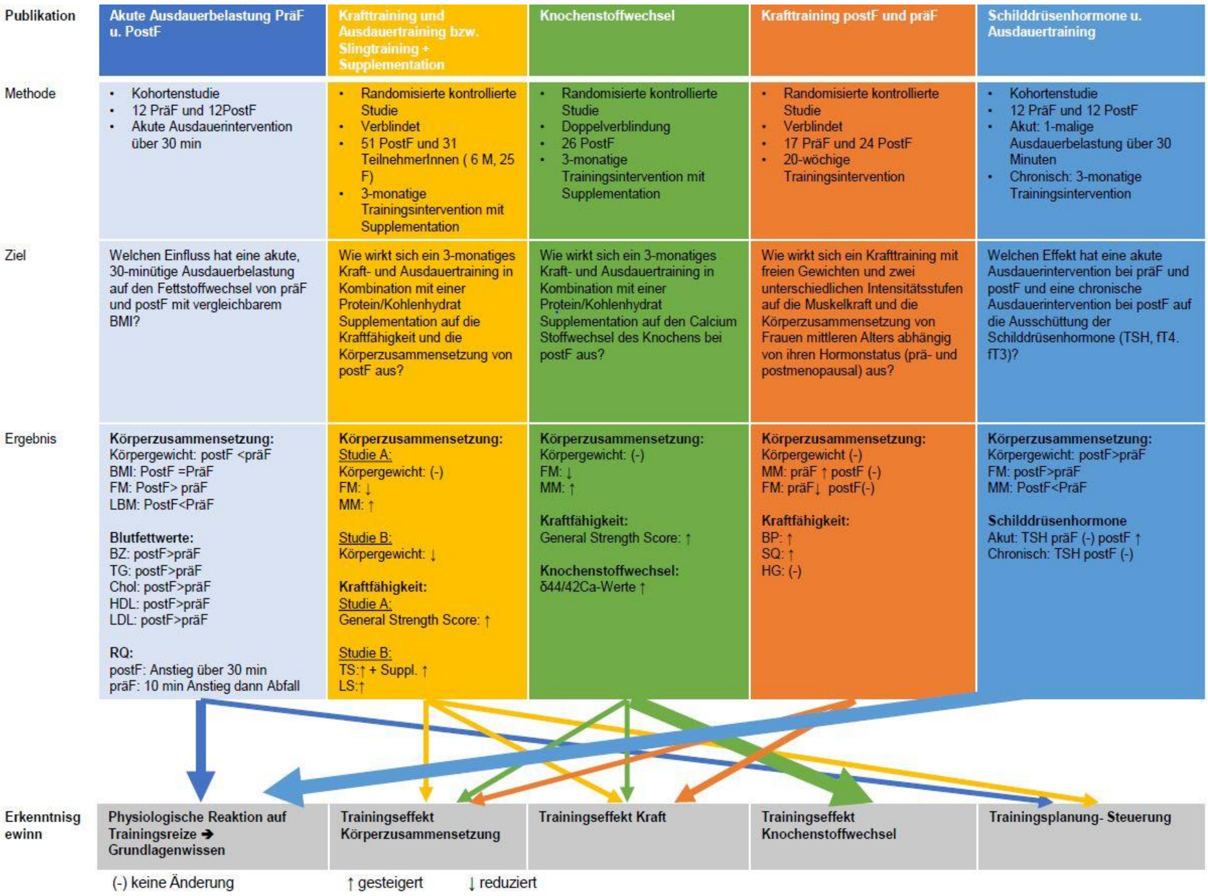

Abbildung 11: Graphische Zusammenfassung der durchgeführten Studien und deren Erkenntnisgewinn

Forschungsfrage 1: Welchen Einfluss hat eine akute, 30-minütige Ausdauerbelastung auf den Fettstoffwechsel von prä- und postmenopausalen Frauen mit vergleichbarem BMI?

In der Untersuchung konnte wie auch schon in anderen Studien gezeigt werden, dass postF mit vergleichbarem BMI wie präF mehr FM, weniger MM und ein höheres Körpergewicht haben [126,127,179]. Ebenso waren die Blutfettwerte bei der postmenopausalen Stichprobe erhöht und deuteten so auf das erhöhte kardiovaskuläre Risiko der Teilnehmerinnen hin [128]. Diese Veränderungen des postmenopausalen Stoffwechsels zeigten sich auch während einer 30-minütigen moderaten Ausdauerbelastung. Die präF zeigten eine physiologische, wie zu erwartende Reaktion des RQ. Dieser stieg innerhalb der ersten 10 Minuten an, um ausreichend Energie mittels Glukosestoffwechsel zu generieren, ab Minuten 10 sank der RQ ab. Dies deutet auf eine Aktivierung des Fettstoffwechsels hin [180,181]. Dem gegenüber zeigten die postF einen konstanten Anstieg der RQ-Werte. Die Frauen waren demnach nicht in der Lage trotz moderater Belastung den Fettstoffwechsel zu aktivieren. Dies hat zur Folge, dass die postF durch moderates Ausdauertraining nicht wie angenommen den Fettstoffwechsel trainieren. Ein Grund dafür ist der durch den E2 Mangel fehlende Einfluss auf die Mitochondrien Membran. Die daraus resultierenden höheren RQ Werte konnten auch andere Autoren zeigen [81,130,131]. Aus der Untersuchung resultiert die Erkenntnis, dass der mit der Menopause einhergehende Mangel an E2 den Fettstoffwechsel der Frauen massiv beeinflusst. Die Folge für die Frauen ist neben dem gestörten Stoffwechsel und dem daraus resultierenden erhöhten Krankheitsrisiko, dass gängige Trainingsempfehlungen nicht zielführend sind. Es müssen daher neue Empfehlungen angepasst auf die Zielgruppe der postF entwickelt werden. Die WHO empfiehlt beispielsweise für alle Erwachsenen bis 65 Jahren 150-300 Minuten aerobes Training bei moderater Intensität oder 75-150 Minuten bei intensiver Intensität pro Woche zur Gesunderhaltung. Zusätzlich sollte mindestens an 2 Tagen pro Woche Krafttraining für alle großen Muskelgruppen betrieben werden [17]. Doch wie die vorliegenden Untersuchungen zeigen, sind diese Empfehlungen nicht geeignet, um den Fettstoffwechsel der postF zu trainieren und so deren Gesundheit zu fördern. Hier sind weitere Studien nötig, um den Effekt von Trainingsinterventionen bei dieser Zielgruppe zu überprüfen. Kritisch betrachtet werden muss die große Altersdifferenz zwischen den beiden Stichproben. Daher stellt sich die Frage, ob die Unterschiede im RQ nicht auf das Alter zurückzuführen sind. Hier wäre beispielsweise eine prämenopausale Gruppe zwischen 40 und 45 Jahren interessant gewesen. Dennoch untermauern andere Autoren [81,129,130] die vorliegende Ergebnisse.

Forschungsfrage 2: Wie wirkt sich ein 3-monatiges Kraft- und Ausdauertraining in Kombination mit einer Protein/Kohlenhydrat Supplementation auf die Kraftfähigkeit und die Körperzusammensetzung von postmenopausalen Frauen aus?

Basierend auf der ersten Studie und den Empfehlungen der WHO [17] wurde aufbauend auf den Ergebnissen aus der Studie von Isenmann et al. [124,125,154] und den älteren aber spezifischeren Empfehlungen des ACSM die Studie unter 4.2 konzipiert [58,60]. Es konnte gezeigt werden, dass ein Training bestehend aus zwei moderaten bis intensiven Ausdauereinheiten (Walking) und einer Krafttrainingseinheit pro Woche zur Steigerung der funktionellen Kraft und zu einer Reduktion des Körperfettes führt. Die Supplementation aus Sauermilchkäse und Brot konnte die Effekte nicht verstärken, auch wenn die Steigerung der Handgriffkraft in der Interventionsgruppe deutlicher war.

Demgegenüber konnte gezeigt werden, dass ein Schlingentraining in Kombination mit einer Protein/Kohlenhydrat Supplementation zu einer Kraftsteigerung und Abnahme des Körpergewichts führt, hier konnte die Supplementation die Kraftzunahme der Rumpfkraft signifikant vergrößern. Auch wenn in beiden Studien dreimal pro Woche trainiert wurde, muss berücksichtigt werden, dass in Studie B kein Ausdauertraining stattgefunden hat und der Fokus auf dem Krafttraining lag. Damit entspricht das Training eher den Empfehlungen des ACSM [60]. In dieser Studie fehlte die Analyse der Körperzusammensetzung, daher ist nur zu vermuten, dass die Gewichtsreduktion auf eine Abnahme der Fettmasse zurückzuführen ist. Die TeilnehmerInnen in Studie B hatten durchschnittlich ein höheres Körpergewicht. Da bekannt ist, dass schwächere bzw. schwere ProbandInnen schneller und deutlicher auf Trainingsreize reagieren als andere kann diese eine Erklärung für die deutliche Adaptation an die Intervention sein. Es zeigte sich auch, dass die TeilnehmerInnen umso schwerer sie waren, umso weniger an Muskelkraft zulegen konnten. Hier könnte eine Ursache in der Trainingsform Schlingentraining liegen. Da das gesamte Körpergewicht gehalten werden muss und gleichzeitig der gesamte Körper stabilisiert werden muss, konnten die schweren TeilnehmerInnen vermutlich nicht so schnell die Unterstützungsfläche verkleinern und so die Intensität steigern [91,182].

Dass die Protein/ Kohlenhydrat Supplementation keinen Effekt in Studie A gezeigt hat liegt vermutlich an methodischen Mängeln. Da die gesamte Studie, während der Covid-19-Pandemie und damit auch unter den entsprechenden Schutzmaßnahmen stattfand, musste anders als in Studie B auf ein gemeinsames Training und die gemeinsame Einnahme des Sauermilchkäses mit Brot verzichtet werden. So konnte nicht überprüft werden, ob die Frauen die Protein/ Kohlenhydrat Nahrung innerhalb von 30 Minuten nach jedem Training zu sich genommen haben, so wie es in Studie B bzw. in der Studie von Isenmann et al. der Fall war [124]. Es musste auf die Compliance der Teilnehmerinnen vertraut werden. Auch die fehlenden Änderungen im Körpergewicht können auf die pandemische Lage zurückgeführt werden. Denn anderes als in den sonstigen Untersuchungen konnte das Ausdauertraining zu jeder Tageszeit durchgeführt werden. So haben einige Teilnehmerinnen nach dem Training den Sauermilchkäse und das Brot als Mahlzeitersatz zu sich genommen und andere habe es zusätzlich gegessen. Anzunehmen ist, dass ernährungsbewusste Frauen eine Mahlzeit ersetzten und andere es eher zusätzlich gegessen haben. Ebenfalls wurde die Ernährung weder vorher noch während der Studie überwacht, somit fehlen

Informationen zur Ernährungsweise und dem Proteinhaushalt der TeilnehmerInnen. In Studie A wurde lediglich die Ernährungsweise abgefragt. In folgenden Studien müsste daher sowohl vor als auch während der Intervention die Ernährung überwacht werden. Für deutlichere Effekte im Bereich des Körpergewichtes und der Körperzusammensetzung sollte eine standardisierte Ernährung angestrebt werden [88]. Ebenso sollte die Supplementation unter Aufsicht und die Trainingseinheiten zur festen Uhrzeit stattfinden. Zudem sollte neben dem Körpergewicht die Körperzusammensetzung analysiert werden. Ebenso sollte neben der Bein-, Brust- und Handkraft auch die Rumpfkraft getestet werden. So kann eine genaue Aussage über die Fitness der TeilnehmerInnen gemacht werden, auch wenn die durchgeführte PCA dafür spricht das alle Kraftwerte im allgemeinen Kraftwert (General Strength Score) repräsentiert wurden. In der vorliegenden Studie wurde die Kraft mittels Wiederholungsmaximum nach Rühl getestet [183]. Zudem gab es Unstimmigkeiten in der Umsetzung, dies führte zur Wiederholung von Tests, was sich wiederum positiv auf den Lerneffekt der Probandinnen auswirkte. Genauer wäre ein 1RM-Test gewesen, in zukünftigen Studien sollte das Protokoll der Krafttestung genauer gestaltet und eine Familarisierungsphase eingefügt werden, um das 1RM zu testen. Dennoch kann sowohl Schlingentraining als auch die Kombination aus Ausdauertraining (2/w) und Krafttraining mit dem eigenen Körpergewicht (1/w) empfohlen werden. Basierend auf den Ergebnissen und der Empfehlung der WHO und der ACSM sollte in einer nächsten Studie die Wirkung von moderatem bis intensivem Ausdauertraining (2/w) und Krafttraining (2/w) mit dem eigenen Körpergewicht und einer Protein/Kohlenhydrat Supplementation bei einem Proteindefizit überprüft werden. Denn alle Probandinnen waren mit großer Begeisterung dabei und haben die gesamte Studienzeit intensiv trainiert, was auch die niedrigen Dropouts zeigen.

Forschungsfrage 3: Wie wirkt sich ein 3-monatiges Kraft- und Ausdauertraining in Kombination mit einer Protein/Kohlenhydrat Supplementation auf den Calcium Stoffwechsel des Knochens bei postmenopausalen Frauen aus?

Die Untersuchung des Knochenstoffwechsels erfolgte bei einer Subgruppe (n=26) aus der Hauptstudie (siehe 4.2). Es konnte auch in dieser Subgruppe eine Kraftsteigerung und eine signifikante Verbesserung des Knochenstoffwechsel erreicht werden. Die hier verwendete Methode der $^{44}Ca/^{42}Ca$ Isotopenanalyse, zeigte sich wie schon bei Eisenhauer et al. [112], als sehr gut geeignet . Sie stellt eine strahlungsarme und wenig aufwendige Alternative zur bis dato verwendeten DEXA- Methode (Dual- Energy-X-Röntgen-Absorptiometry) dar. Obwohl das Training nicht explizit für die Verbesserung des Knochenstoffwechsel konzipiert war, konnte dieser trotzdem signifikant verbessert werden. Mit einer Anpassung des Trainings in Form einer Steigerung des Krafttrainings wären sicherlich noch größere Effekte möglich gewesen [106,111,184,185]. Daher sollte bei einer, wie unter Fragestellung 2.3 vorgeschlagenen Untersuchung wieder der Knochenstoffwechsel mit untersucht werden. Da es sich um eine Subgruppenanalyse handelt, wird hier nicht erneut auf die methodischen Fehler in Bezug auf die Proteinsupplementation und das fehlende Monitoring der Nahrung eingegangen. Trotz der methodischen Schwächen kann abschließend festgehalten werden, dass sich eine Trainingskombination mit Kraft- und Ausdauertraining positiv auf den Knochenstoffwechsel der postF auswirkt und die gewählte Untersuchungsmethode sehr gut geeignet ist.

Fragestellung 4: Wie wirkt sich ein Krafttraining mit freien Gewichten und zwei unterschiedlichen Intensitätsstufen auf die Muskelkraft und die Körperzusammensetzung von Frauen mittleren Alters abhängig von ihren Hormonstatus (prä- und postmenopausal) aus?

In dieser Untersuchung wurde der Fokus auf das Krafttraining mit freien Gewichten in zwei verschiedenen Intensitätsbereichen gelegt. Da die Studie zeitgleich mit der 2. Fragestellung bearbeitet wurde, wurde auch hier die Ernährung nicht überwacht. Das stellt auch hier eine Limitation dar. Dennoch konnte gezeigt werden, dass sich auch mit reinem Krafttraining die funktionelle Kraft bei postF signifikant verbessern lässt. Auch in dieser Studie waren die Frauen hoch motiviert und zeigten großes Interesse an der Teilnahme. Da die Frauen, wie auch in der Vorstudie und in anderen Studien angaben, wenig Zeit für die eigene Gesundheit neben den Familienaufgaben zu haben, wurde das Training auf zweimal 30 Minuten geplant [186]. Mit einem größeren Umfang wären vermutlich größere Effekte möglich [157].

Anders als die Studie, die unter 2.2 vorgestellt wurde, wurde keine Verbesserung der Griffkraft nachgewiesen, obwohl das Halten der Gewichte diese erforderte. Die Griffkraft gilt häufig als ein Indikator für den Muskelstatus, die Gesundheit und Mortalität von Älteren [161,162] und ist daher eine wichtiger Parameter. Die Teilnehmerinnen (54,3 ±4,7/ 55,6 ±2,9 Jahre) waren auch nur wenige Jahre jünger als die Kohorte aus Studie 2.2 (57,5± 4,3 Jahre). Somit ist nicht davon auszugehen, dass das Alter den fehlenden Effekt erklärt. Eine Hypothese könnte sein, dass nicht nur das Greifen die Griffkraft verbessert, sondern das Zusammenspiel von stabilem Rumpf und Armmuskeln und das dieses Zusammenspiel eher bei funktionellen bzw. Übungen mit dem eigenen Körpergewicht als mit dem Training an Maschinen oder freien Gewichten erreicht wird [160]. Die nur minimalen Veränderungen in der Körperzusammensetzung können auf eine fehlende Ernährungsintervention oder einen zu geringen Trainingsreiz während der 12 wöchigen Intervention zurückzuführen sein [41,126]. Zudem fehlte eine Ausdauerintervention die den Fettstoffwechsel hätte trainieren und Triglycerid Speicher hätte leeren können [76,91,93].

Fragestellung 5: Welchen Effekt hat eine akute Ausdauerintervention bei prä- und postmenopausalen Frauen und eine chronische Ausdauerintervention bei postmenopausalen Frauen auf die Ausschüttung der Schilddrüsenhormone (TSH, fT4. fT3).

Die unter 4.5 vorgestellte Studie stand nicht im Fokus dieser kumulativen Dissertation. Dennoch ist der Zusammenhang von Menopause und Auftreten der Störungen der Schilddrüse sehr relevant. Bei vielen Frauen ist oft nicht klar und häufig auch nur schwer zu ergründen, ob die Symptome der Menopause oder einer Schilddrüsenstörung zuzuordnen sind [36,37]. Bei der Vielzahl der Symptome und dem Zusammenspiel der verschiedenen Regelkreise im Hormonsystem ist es aber notwendig, die Reaktion der Schilddrüse auf Trainingsinterventionen hin zu kennen, um allen postF geeignete Empfehlungen geben zu können. In der vorliegenden Untersuchung konnten, keine Unterschiede in der Konzentration der Schilddrüsenhormone (TSH, fT3, fT4) zwischen präF und postF gefunden werden. Bei der Deutung dieser Ergebnisse muss die sehr geringe Stichprobe der Pilotstudie berücksichtigt werden. In anderen Untersuchungen konnte ein altersabhängiger TSH-Anstieg gezeigt werden [187]. Die TSH Erhöhung, bedingt durch einen akuten Ausdauerreiz, konnte nur bei der prämenopausalen Kohorte signifikant nachgewiesen werden. Dies konnten auch andere Autoren zeigen [167,168,171]. Bei den postF war dieser vor der Intervention deskriptiv zu sehen, nach der Intervention war dieser aber nicht mehr nachzuweisen. Der geringe Anstieg kann eventuell mit der verlangsamten Reaktion des Stoffwechsels auf den Belastungsreiz zusammenhängen. Dies müsste aber weiter überprüft werden. Physiologisch ist der Anstieg durch den gesteigerten Ruheumsatz unter Belastung zu erklären [188]. Wie in der unter 4.1 vorgestellten

Studie zeigen sich hier aber deutliche Unterschiede zwischen präF und postF. Die veränderte Reaktion nach der Ausdauerintervention lässt sich auf eine zumindest im Tierexperiment nachgewiesene verstärkte Expression von Schilddrüsenhormonrezeptoren erklären [174]. Hierzu fehlen aber Daten aus Untersuchungen am Menschen. In einer erneuten Studie zur Überprüfung der Trainingsparameter sollte ebenfalls der Schilddrüsenstatus erhoben werden, um weitere Erkenntnisse zur hormonellen Reaktion bei postF zu erlangen.

6. Fazit und Ausblick

Die im Rahmen dieser kumulativen Dissertation erhobenen Daten liefern wichtige Erkenntnisse zum Umgang mit postmenopausalen Beschwerden und der Reaktion des weiblichen Stoffwechsels auf verschiedene Trainingsinterventionen. Ableitend aus den Daten kann aktuell den Frauen eine Kombination aus Ausdauer- und Krafttraining empfohlen werden, um Muskelmasse, funktionelle Kraftfähigkeit und den Knochenstoffwechsel zu verbessern. Unter Berücksichtigung der methodischen Mängel sollte eine Protein/Kohlenhydrat Supplementation nur nach vorheriger Überprüfung des Proteinhaushaltes durchgeführt werden. Besonders wertvoll ist die Erkenntnis, dass ein Training bestehend aus moderatem bis intensives Walking (60 min, 2x/w) und einmaligem Krafttraining mit dem eigenen Körpergewicht (60 min) auch den Knochenstoffwechsel positiv beeinflusst. Hier sollte unbedingt eine längere Studie durchgeführt werden, um die langfristigen Effekte zu überprüfen. Die Griffkraft scheint am besten durch eine Kombination aus Ausdauer- und Bodyweight Training gesteigert zu werden, wohingegen die Rumpfkraft von einem Schlingentraining mit Protein-/Kohlenhydrat Supplementation profitiert. Die Fettmasse, die ein wichtiger Faktor für die kardiovaskuläre Gesundheit darstellt, sollte in folgenden Studien genauer beispielsweise mittel BIA und Atemgasanalyse überwacht werden. Auch ein reines Krafttraining mit freien Gewichten wirkt sich positiv auf die funktionelle Kraftfähigkeit aus, allerdings nicht auf die Körperzusammensetzung, kann aber auch als Mittel gegen den altersbedingten Muskelmasseabbau empfohlen werden.

Abschließend ist zu sagen, dass die Teilnehmerinnen trotz vieler familiärer und beruflicher Verpflichtungen sowie einer andauernden COVID-19-Pandemie sehr motiviert und engagiert bei den Studien mitgewirkt haben und viele das Training fortführen. Hier zeigte sich ein online-basiertes Training und die Supervision mittels Wearables als hilfreich. Alle Teilnehmerinnen gaben an deutlich an Fitness gewonnen zu haben. Dafür sprechen die gesteigerten Kraft- und Muskelwerte sowie bisher nicht veröffentlichte Daten der Laktatstufentests nach der Intervention.

In zukünftigen Studien sollte die Wirkung von moderatem bis intensivem Ausdauertraining (2/w) und Krafttraining (>2/w) mit dem eigenen Körpergewicht und einer Protein/Kohlenhydrat Supplementation bei einem bestehenden Proteindefizit überprüft werden. Das Krafttraining sollte zwei- bis dreimal bzw. mehr als 8 Sets pro Woche beinhalten und mit einer Intensität größer als 50 % des 1 RM durchgeführt werden. Ergänzend sollten sowohl das $^{44}Ca/^{42}Ca$ Verhältnis, zur Bestimmung des Knochenmetabolismus, als auch die Schilddrüsenhormone zum weitere Erkenntnisgewinn erhoben werden.

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8. Anhang - Original Publikationen

Die Publikation „Effects of Acute Aerobic Exercise on Fat Metabolism in Pre- and Postmenopausal Women of Comparable Body Mass Index“ gedruckt mit freundlicher Genehmigung der Autoren und der Deutschen Zeitschrift für Sportmedizin, aus: Hofmann et al. Effects of Acute Aerobic Exercise on Fat Metabolism in Pre- and Postmenopausal Women of Comparable Body Mass Index. Dtsch Z Sportmed. 2022; 73: 235-240

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ORIGINALIA

Effects of Acute Aerobic Exercise on Fat Metabolism in Pre- and Postmenopausal Women of Comparable Body Mass Index

Effekte einer akuten Trainingsbelastung auf den Fettstoffwechsel von prä- und postmenopausalen Frauen mit vergleichbarem BMI

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Summary

› **Problem:** With menopause, the risk of cardiovascular diseases (CVD) increases significantly. A possible molecular mechanism is an estrogen-related change in fat metabolism. Endurance training has been demonstrated to reduce the risk of CVD and to have an impact on fat metabolism (FM). This study aims to analyze the ability of pre- (preW) and postmenopausal women (postW) of comparable body mass index (BMI) to activate their FM during endurance training.

› **Methods:** 12 preW and 12 postW were included. Serum Triglyceride, LDL, HbA1C, estradiol and body composition data were determined. The respiratory quotient (RQ) was determined during moderate 30-minute exercise (60% of the 4 mmol threshold) on an ergometer.

› **Results:** While the BMI of preW and postW was comparable, body fat (BF) (p=0.001), lean body mass (LBM) (p=0.001) and abdominal girth (AG) (p=0.003) were significantly different. Significant group effects could also be identified in HbA1c (p=0.001), cholesterol (p=0.001) and LDL (p=0.000) serum concentrations. RQ decreased during 30 minutes of cycling in preW and increased in postW (p=0.010) over time.

› **Discussion:** The higher AG and BF and the lower LBM demonstrates the change in body composition in postW. An accumulation of fat, especially in the trunk region, goes along with an increase of CVD in postW, even with a normal BMI.

› **Conclusion:** It is evident that postW show altered lipid metabolism compared to preW.

Zusammenfassung

› **Problem:** In der Menopause steigt das Risiko für kardiovaskuläre Erkrankungen (CVD) bei Frauen an. Ein Grund ist der durch die Estrogenabnahme veränderte Fettstoffwechsel (FS). Ausdauertraining kann das Risiko für CVD reduzieren und sich positiv auf den FS auswirken. Das Ziel der Studie ist, es die Fettstoffwechselfähigkeit von prä- (präF) und postmenopausalen Frauen (postF) mit vergleichbarem BMI während einer akuten Ausdauerbelastung zu analysieren.

› **Methode:** 12 präF und 12 postF wurden in die Studie eingeschlossen. Im Blut wurden die Parameter Triglyceride, LDL, HbA1C und Estradiol erhoben. Die anthropometrischen Daten und die Körperzusammensetzung wurde ermittelt. Während 30 Minuten (60% der 4mmol Schwelle) Belastung auf dem Fahrradergometer wurde der Respiratorische Quotient (RQ) erhoben.

› **Ergebnis:** Während der BMI von präF und postF vergleichbar war, unterschieden sich Körperfett (KF) (p=0,001), Magermasse (p=0,001) und Bauchumfang (p=0,003) signifikant. Signifikante Gruppeneffekte konnten auch bei den Serumkonzentrationen von HbA1c (p=0,001), Cholesterin (p=0,001) und LDL (p=0,000) festgestellt werden. Der RQ verringerte sich bei präF und stieg bei postF (p=0,010) an.

› **Diskussion:** Der höhere Bauchumfang und das Körperfett und die niedrige Magermasse zeigen die Veränderung der Körperzusammensetzung. Eine Anhäufung von Fett, vor allem im Rumpfbereich, geht mit einer Zunahme von CVD bei postF einher, auch bei normalen BMI.

› **Konklusion:** Es zeigt sich das postF im Vergleich zu präF einen veränderten Fettstoffwechsel aufweisen.

KEY WORDS:
Menopause, Cardiovascular Risk Factor, Aerobic Training, Metabolism

SCHLÜSSELWÖRTER:
Menopause, kardiovaskuläres Risiko, aerobes Training, Stoffwechsel

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Introduction

Cardiovascular diseases (CVD) are still one of the most frequent causes of death for women worldwide (7). In women the individual risk for this diseases increases significantly with menopause (5). The moment of natural menopause is variable and occur for most women on average around the age of 51 to 52. After menopause, the prevalence for CVD increases significantly. Böhm et al. (4) have evaluated that a rate of 39.0 heart attacks per 100000 women occurs in the age of 45 to 49, but there are 95.1 events per 100000 in the age of 50 to 54 years. Similar data are available for nearly all kinds of CVD and is mechanistically believed to be directly associated with the decrease of estrogen serum concentrations in postmenopausal women (5). A possible molecular mechanism discussed is an estrogen related ›

Table 1

Body composition.

	PRE-MENOPAUSAL (N=12)		POST-MENOPAUSAL (N=12)		P-VALUE
	M	SD	M	SD	
Age (years)	25.0	3.5	57.7	4.3	0.001
Weight (kg)	67.6	9.1	64.1	4.9	0.378
BMI (kg/m²)	23.0	2.3	23.6	1.3	0.444
Abdominal girth (cm)	76.2	7.4	85.1	5.5	0.003
Fat mass (%)	27.9	3.9	34.0	2.4	0.001
Lean body mass (LBM) (%)	72.9	3.9	65.9	2.4	0.001
Body cell mass (BCM) (%)	27.6	3.2	21.9	1.5	0.001

Table 2

Blood parameters. HbA1C=haemoglobin A1c; TG=triglycerides; CHOL=cholesterol; HDL=high-density lipoprotein; LDL=low-density lipoprotein; [a]=-Mann-Whitney-U-Test; [b]=T-test for independent samples.

	PRE-MENOPAUSAL (N=12)		POST-MENOPAUSAL (N=12)		P-VALUE
	M	SD	M	SD	
Blood sugar [mg/dl]	90.7	4.9	98.7	6.2	0.002[a]
HbA1c [%]	5.1	0.2	5.5	0.2	0.001[b]
TG [mg/dl]	64.6	16.6	80.7	29.5	0.178[b]
CHOL [mg/dl]	162.6	23.3	243.9	36.0	0.001[a]
HDL [mg/dl]	59.5	9.2	72.9	12.5	0.007[a]
LDL [mg/dl]	90.3	18.1	154.2	34.7	0.001[a]

change in the fat metabolism of postmenopausal women (14). In animal experiments (11, 19, 20) and in human intervention studies (15) it could be demonstrated that fat metabolism is directly influenced by 17 beta-estradiol. Therefore, there is need for strategies to treat postmenopausal complains, especially for the prevention of CVD and metabolic diseases. A powerful factor of huge impact on metabolism is physical activity. There are numerous studies demonstrating the beneficial effects of exercise in the prevention and therapy of the metabolic syndrome (13, 16). Risk factors correlated to CVD, like serum cholesterol or the high density lipoprotein/ low density lipoprotein (HDL/LDL) ratio are negatively influenced by the decrease of estrogens and can be significantly improved by exercise (18). Interestingly, in animal experiments it was shown that a decrease in serum estradiol results in a reduction of movement drive (20). There are indications that this effect also occurs in postmenopausal women (8, 12). So, the decrease of estrogen serum concentrations in postmenopausal women may have a double negative impact on the cardiovascular system a) directly by a modulation of metabolism and b) indirectly via the reduced motivation for movement.

To develop new individualized therapeutic concepts for the prevention of cardiovascular and metabolic diseases in postmenopausal women, knowledge about the mechanisms involved in the metabolic changes during menopausal transition is important. Therefore, it was the aim of this study to investigate the metabolic response of pre- and postmenopausal women of comparable body mass index (BMI) during low intensity endurance training on a bicycle ergometer.

Material and Methods

Preparticipation Examination

Each women completed 3 days of testing. The study has been conducted in line with the ethical principles set up in the Declaration of Helsinki. All participants received detailed oral and written information about the study before inclusion, and all gave written informed consent to participate. Approval for the experimental study was obtained from the Ethics Committee of the German Sport University Cologne.

For inclusion all pre- and postmenopausal women were healthy, non-smoker, had a BMI lower than 25 and were free of performance limited illnesses and metabolic diseases. No participant took any medication that effect fat metabolism. All attending women had no cancer in history. PreW had to show a regular cycle and no pregnancies. All examinations of PreW were planned in the middle of their menstrual cycle. None of the participants were athletes, all performed less than two hours of endurance training per week. Estradiol and FSH were analyzed to ensure that the women were pre- or postmenopausal and not taking hormone supplements. While examination anthropometric parameters were determined. Body composition was measured by bio-electrical impedance analyses using Body Explorer (Kommunikation & Service GmbH, Frankfurt, Germany).

T1

Before training blood serum concentration of cholesterol (CHOL), high density lipoprotein (HDL), low density lipoprotein (LDL), Triglyceride (TG), blood sugar and HbA1c were determined. The participants underwent a lactate threshold test by means of spiroergometric examination according to the Hollmann-Venrath-scheme by using ergoselect 200P (Ergoline GmbH, Bitz, Germany). At rest and after each stage lactate level, heart rate and BORG stage was determined. The load for the second testing day was determined based on the data collected, by using threshold calculation according to Mader.

T2

During 30-minute load at 60% of the 4mmol threshold on the bicycle ergometer, another spiroergometric examination was carried out. Spiroergometric parameters like, RQ, $\dot{V}O_2$ [l/min] $\dot{V}CO_2$ [l/min] and $\dot{V}O_2$ peak ml/(kg*min) was continuously recorded. Furthermore, heart rate was measured and lactate was collected at minute 10, 20 and 30.

Statistical Analyses

The data collected were used to test for normal distribution using the Kolmogorov-Smirnov test. In the case of a normal distribution, the arithmetic mean values were compared with each other using the t-test for independent samples. If no normal distribution was present, the nonparametric Mann-Whitney U-test was calculated. The current version of SPSS (IBM SPSS Statistics Version 24.0.0.0) was used. By using the Levene-test the equality of error variances was checked and variance homogeneity was assumed for a probability of error $p>0.05$.

Results

Anthropomorphic Data

12 postW (57.7±4.3) and 12 preW (25.0±3.5) finished the study. During the study 2 PreW had to be excluded. The last menstruation of PostW was 5 to 7 years ago. The BMI of both groups was nearly identical (23.0±2.3 premenopausal; 23.6±1.3 postmenopausal), abdominal girth (AG) (76.2±7.4 cm premenopausal;

85.1±5.5 cm postmenopausal), body fat mass (BF) (27.9±3.9% premenopausal; 34.0±2.4% postmenopausal) and lean body mass (LBM) (72.9±3.9 premenopausal; 65.9±2.4 postmenopausal) showed significant differences (table 1).

Metabolic and Cardiovascular Risk Factors:

Differences in blood parameters between preW and postW could be found for all parameters (table 2). Statistically significant differences could be demonstrated for HbA1c (p=0.001), CHOL (p=0.001) and in LDL concentration (p=0.000).

Metabolic Response during Low Intensity Training

Parameters of all participants related to physical performance showed significant differences. The maximum power was 195±35.9 watts in the preW and 119.2±17.6 watts in the postW while performance at 60% of 4mmol lactate threshold was 88.8±27.1 watts in preW and 59.3±13.7 watts in postW (table 3).

Group differences in the lactate serum concentrations during exercise could be detected after 10, 20 and 30 minutes. In the preW lactate increased during the first 10 minutes of exercise, stay constant until 20 minutes and decreased after 30 minutes. In postW, lactate increased strongly during the first 10 minutes of exercise and keeps on these high levels during the completed exercise period (table 4; figure 1).

RQ in rest was not different between both groups and increased strongly in the first 10 min of exercising. Interestingly, in preW after 20 minutes the RQ decreased. In contrast in the postW, there was a constant increase in RQ over the 30-minute load.

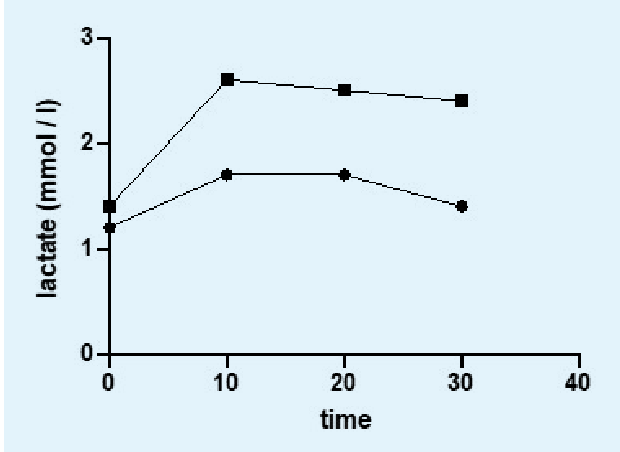

Figure 1

Lactate for 30 minutes endurance exercise. Dots=premenopausal; squares=postmenopausal.

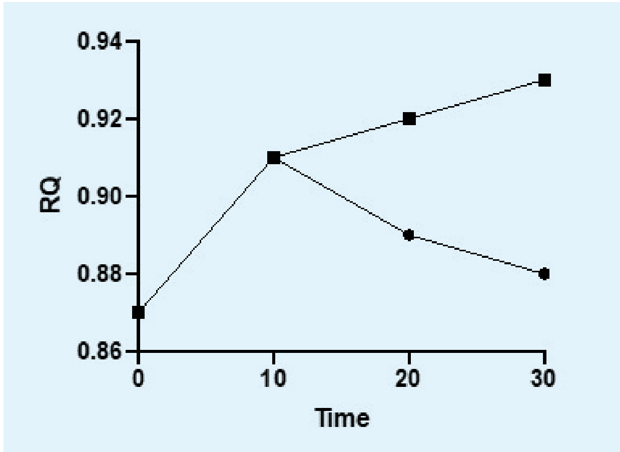

Figure 2

RQ for 30 minutes endurance exercise. Dots=premenopausal; squares=postmenopausal.

Discussion

With menopause, a variety of physiological changes and complaints become apparent in women. With respect to fat metabolism it is of relevance that most women are suffering by weight gain (nearly 0.5kg/year) and abdominal obesity while menopausal transition (10). In our study we investigated preW and postW of comparable BMI (table 1) and a normal body weight. Nevertheless, postW show higher TG, CHOL, and LDL levels at baseline measurement. Interestingly, in postW the measured diameter of AG and BF was significant higher compared to the preW, whereas LBM was significantly lower. This impressively demonstrates the change in body composition in postW although they are per definition of regular body weight. These observations are in line with findings of Chen et al. (6) and Greendale et al. (9) who showed that an accumulation of fat, especially in the trunk region goes along with an increase of CVD in postW, even with a normal BMI. Abildgaard et al. (1) shows that at menopause trunk fat increased while leg fat decreased. We were also able to measure higher AG in the postW, too.

The postW showed significantly higher serum concentrations of blood sugar, HbA1c, CHOL, HDL and LDL compared to the preW (table 2). These results are consistent with other studies. Pu et al. showed higher cardiovascular indicators like triglycerides, LDL cholesterol and fasting glucose in postW (15).

The RQ at rest shows no significant differences between both groups. Exercises results in both groups within the first ten minutes in an increase of the measured RQ (post 0.91±0.03 vs. pre 0.91±0.03), what can be explained by an increased utilization of carbohydrates for energy supply. As expected, the RQ in preW decreases after 20 minutes. This can be explained by an increased utilization of fat as energy supplier, because of the moderate training intensity. This indicates that moderate aerobic exercise results in an increased lipolysis in preW (3). In our postW, even after 30 min no decrease of the RQ was detectable. RQ after 20 min exercise was significantly higher in postW, compared to preW (table 5, figure 2).Even after 30 minutes, energy production in postW seem to delay mainly on carbohydrates (RQ: post 0.93±0.04 vs. pre-0.88±0.04). Since these results are significant, it can be assumed that postW are not able to activate their fat metabolism as an energy supplier when exposed to a 30-minute moderate load, as preW do. These data indicate that the different hormone status seems to have a negative impact, not only on the blood lipid values, but also on the utilization of the fat metabolism during exercise. One explanation could be that estrogens have a direct influence on the mitochondrial membrane and influence bioenergetic function of mitochondria. The lipid tolerability could therefore be influenced by the reduced estrogen level (1, 17). Abildgaard et al. (2) were able to show that postW have higher RQ during a 45-minute exposure compared to preW. Furthermore, postmenopausal women were shown to have 33% lower whole-body fat oxidation. A high whole-body fat oxidation correlated with a low visceral fat percentage. In the data presented here, preW show a lower body fat percentage than postW, according to Abildgaard et al. (2).

Our detected lactate serum concentrations during exercise support these findings. Starting from comparable concentrations in rest in both groups, during exercise lactate serum ›

Table 3

Parameters related to physical performance.

	PREMENOPAUSAL (N=12)		POSTMENOPAUSAL (N=12)		P-VALUE
	M	SD	M	SD	
Watt max. [Watt]	195.0	35.9	119.2	17.6	0.001
Performance at 60% 4mmol lactate [Watt]	88.8	27.1	59.3	13.7	0.005

Table 4

Lactate for 30 minutes endurance exercise

	TIME	PREMENOPAUSAL (N=12)		POSTMENOPAUSAL (N=12)		P-VALUE
		M	SD	M	SD	
Lactate [mmol/L]	rest	1.2	0.6	1.4	0.3	0.272
	10`	1.7	0.7	2.6	0.8	0.010
	20`	1.7	0.7	2.5	1.0	0.025
	30`	1.4	0.5	2.4	1.1	0.011

Table 5

Respiratory quotient for 30 minutes endurance exercise.

	TIME	PREMENOPAUSAL (N=12)		POSTMENOPAUSAL (N=12)		P-VALUE
		M	SD	M	SD	
RQ	rest	0.87	0.04	0.87	0.05	0.885
	10`	0.91	0.03	0.91	0.03	0.750
	20`	0.89	0.04	0.92	0.03	0.036
	30`	0.88	0.04	0.93	0.04	0.010
RQ [%]	10`-30`	-3.7	4.1	+1.3	4.2	0.011

concentrations increase more significantly in postW (table 4). Lactate is produced as an end product of anaerobic glycolysis. A continuously increase of lactate confirms the increased utilization of carbohydrates as energy sources (2).

In summary the data of our study underline findings demonstrating that estradiol has a huge impact on the fat metabolism (4). Our postW had significantly reduced estrogen levels (post 19.0±0.0 pg/ml vs. pre 134.8±103.4 pg/ml). A decrease in estradiol leads to a reduced fat oxidation rate in animal experiments (11, 19, 29). The results of RQ and lactate values indicate a reduced fat metabolism rate in postW too and thus confirm the influence of estradiol on the fat metabolism of women. This aspect needs to be considered in the development of training concepts for postW. Training concepts need to be depended to the different kinetics in fat metabolism in postW. The recommendations for short (<30 Minutes) moderate aerobic exercise, as a promoter of fat metabolism seems not suitable for women after menopause.

The age effect must be viewed critically. The group of preW was represented by young women (age: 25.0±3.5 years). Thus, the influence of age on the differences in body composition, blood values and stress test data cannot be dismissed.

Nevertheless, our data and findings that there is a deterioration of fat metabolism with decrease of estradiol correspond to those of other authors (1, 2, 3, 5). The influence of age, and thus the difference in performance, can be neglected with regard to the data of RQ and lactate, since the load measurement was carried out based on the individual performance level. According to the differences in performance, differences in the reaction of the fat metabolism were shown.

Conclusion

It seems necessary to develop individualized training concepts accorded on the individual metabolic status and abilities of postW. The data show that postW accumulate more FM and have more harmful blood lipid levels compared to preW at the same BMI. In postW no shift from carbohydrate to fat metabolism was detected via endurance exercise. Therefore, their deficient ability to reach fat metabolism seems to be an important key factor in the development of new training regimes for postW.

Conflict of Interest

The authors have no conflict of interest.

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nutrients

Article

Combinatory Effects of Training and Nutritive Administration of Carbohydrates and Protein via Food on Strength in Postmenopausal Women, and Old Men and Women

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Abstract: The age-related loss of muscle mass promotes many impairments. Training and protein supplementation are suggested to prevent muscle wasting, but recommendations for all populations are not based on scientific evidence. This study combines protein/carbohydrate supplementation (PCS) and training for seniors and postmenopausal women. Project A: 51 postmenopausal women (PMW, 57.3 ± 3.0 years old) underwent health-oriented training (12 weeks, moderate-strength training + moderate-endurance training). The intervention group (IG) additionally received 110 g sour milk cheese (SMC) and toast. Project B: 25 women and 6 men (65.9 ± 4.9 years old) performed intense sling training (12 weeks). The IG additionally received 110 g SMC, toast, and buttermilk. Strength was tested before and after in both studies. Project A: there was significant increase in strength, no additional effect of PCS, and a reduction in body fat in the controls. Project B: there was significant increase in strength, significant additional effects of PCS for trunk strength, and a significant reduction in body weight. Combining training and PCS may counteract strength loss. Combined endurance/resistance training is recommended to PMW for whom the benefits of PCS are restricted. Aged subjects may benefit from PCS when training intensely, but these benefits may be strongly individual.

Keywords: protein/carbohydrate supplementation; sling training; endurance training; strength training; BMI

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1. Introduction

Aging is accompanied by a variety of physical changes, such as a decrease in muscle mass up to sarcopenia, an increase in cardiovascular diseases, and frailty syndrome. In women, the onset of menopause or menopausal transition plays a role. Likewise, the massive decrease in estradiol supports the decrease in muscle mass and promotes the development of sarcopenia [1–3]. The likelihood of metabolic diseases such as Type 2 diabetes mellitus and metabolic syndrome also strongly increases [1,4]. There are numerous studies demonstrating the beneficial effects of exercise in the prevention and therapy of muscle mass loss, sarcopenia, metabolic syndrome, and risk for cardiovascular diseases [5–11].

The reduction in muscle mass during aging is due to a decrease in physical activity, and an imbalance between muscle-protein synthesis and breakdown. This can lead to the development of sarcopenia [10,12], which negatively impacts the functional capacity and quality of life of affected persons [12,13]. The revised 2019 version of the guidelines of the European Working Group on Sarcopenia in Older People (EWGSOP) emphasizes muscle strength as the main determinant, as it is best suited for predicting the adverse outcomes of sarcopenia [14]. Naseeb and Volpe summarized that protein supplementation and long-term aerobic exercise reduce the age-related loss of muscle strength [15]. An age-related decrease in muscle mass, even if it cannot be defined as sarcopenia, is a general risk in the aging population [15,16] that menopause promotes [16]. Avoiding a decrease in muscle mass and strength with physical training [17] is important for the prevention of a variety of age-related diseases. Aging is often accompanied by a decrease in physical activity [10]. In many cases, musculoskeletal disorders such as osteoarthritis cause this [17,18], but there are various additional reasons, including psychological ones [19,20]. Untreated, these impairments lead to an increased risk of becoming frail. Frailty syndrome is characterized by reduced activity and gait speed, a decrease in body strength, fatigue, and weight loss. Sarcopenia, stroke, myocardial infarction, arterial hypertension, and diabetes mellitus are closely related to the syndrome. A reduction in risk factors, and endurance, strength, and coordination training affect the risk of frailty syndrome [8]. The beneficial effects of physical activity on the maintenance of skeletal muscle mass are supported with protein supplementation [10]. There is a difference between protein supplementation that aims to compensate for the lack of protein intake through a normal diet and a situation with higher protein needs. The first scenario is typical for geriatric or cachectic individuals [21]. The adequate plasma levels of essential amino acids have a positive effect on muscle protein synthesis [22]. Chronic inflammatory processes that are exacerbated in old age by the decrease in estrogen and the increase in visceral adipose tissue favor proteolysis over protein synthesis. Thus, the breakdown of dietary proteins is imbalanced with the formation of new proteins from amino acids in cells. The result is an increased demand for proteins for equivalent and sufficient muscle protein synthesis in older adults [21,23]. A 2015 data analysis conducted by Gregorio et al. on postmenopausal women identified that about 25% of the population had lower protein intake than the daily recommendation [24]. This same subgroup showed a significant limitation in upper- and lower-extremity functionality. However, for the majority of postmenopausal women and older individuals, protein via supplementation is not needed as a strategy to compensate for a lack of protein uptake. Nevertheless, protein uptake in such individuals, as in younger ones, can support the functional adaptation of the skeletal muscle to a training stimulus [25]. After exercise, the intake of an additional 20–25 g of protein is recommended [21]. Amino acid availability shows a positive effect on muscle development, lean and muscle mass, and muscle strength. Likewise, it increases the plasma concentrations of IGF-1. Protein intake also positively influences calcium absorption and, thus, supports bone health [2]. Studies showed that the combined intake of proteins and carbohydrates leads to higher glycogen storage in the skeletal muscle, and a higher increase in blood sugar and insulin concentration than those of just carbohydrate combinations [26]. The increase in serum insulin levels entails the binding of insulin to IGF-1 receptors, which stimulates muscle protein synthesis in the skeletal muscle and the uptake of amino acids into skeletal muscle cells via various processes [27]. Isenmann et al. compared the intake of a protein/carbohydrate combination via shakes and natural foods by directly following a workout with regard to the regenerative effect on the muscles. The results showed that shakes and supplementation via a natural protein source could equally reduce muscle damage after exercise, and insulin was involved in the regenerative effects [27]. Lichtenberg and colleagues showed that training with protein supplementation using powders also resulted in significant muscle and strength gains in sarcopenic seniors [28]. In those studies, however, supplementation was always via powders or capsules and never via food. In addition, the studies in the available reviews were not consistent. Different supplements, compositions, and time points were used [29,30]. Trommelen et al. indicated that age, and the type and timing of supplementation play a decisive role, so supplementation should be specifically adapted to, for example, age [31]. Eating dairy products and white bread has proregenerative effects on skeletal muscle after exercise [32]. On the basis of the work of Diel and colleagues, and Isenmann and colleagues, this study examines whether the combined uptake of protein and carbohydrates directly after training from natural protein sources could also result in an increase in training adaption, mainly muscle strength, in postmenopausal women and old individuals.

2. Materials and Methods

2.1. Study A: Effect of Training and Protein/Carbohydrate Supplementation in Postmenopausal Women

2.1.1. Study Design and Participants

The study was a randomized intervention with 2 (CG and IG) parallel groups. We recruited 58 women between 50 and 65 years old in Germany by using personal contacts, calls on social media, gynecologists as gatekeepers, or the newsletter of the German Menopause Society (Figure 1). The sample size was determined on the basis of preliminary studies by Wacker [33]. The study started in January 2021 and was completed in November 2021. All examinations took place at the German Sport University, Cologne under the current valid COVID-19 protection regulations. Inclusion criteria were postmenopausal status, and the last menstrual period had to have been at least two years earlier. Exclusion criteria were hormonal diseases, metabolic diseases, cardiac arrhythmias requiring treatment, and limiting neurological, muscular, degenerative, or gastrointestinal diseases. Participants with a history of cancer within the past 5 years were excluded. Unbalanced diets such as vegan diets, smoking, and hormonal substitutions of any kind were excluded. All women had a low-to-moderate fitness status and none of them exercised more than twice per week in terms of strength or endurance training. Prior to recruitment, the approval of the ethics committee of the German Sport University, Cologne (number 008/2021) was obtained, and the study was registered in the German Clinical Trials Register, number DRKS-ID: DRKS00024144. The study protocol was in accordance with the Declaration of Helsinki. After the study procedure had been communicated via telephone, and the inclusion and exclusion criteria had been checked, the women received all information in paper form. Subsequently, an appointment was booked to sign the informed consent form, clarify questions, and start with the examinations. All 63 participants signed the informed consent form.

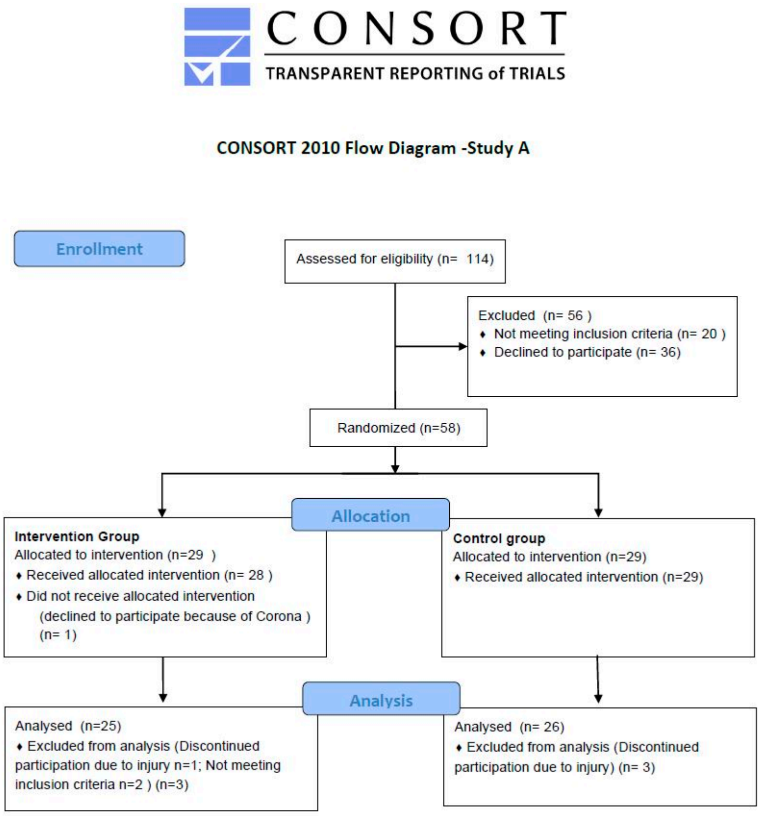

Figure 1. Consort flow diagram—Study A.

2.1.2. Test Day

All participants fasted, with their last meal 12 h before the examination. After the blood samples had been collected, anthropometric data (weight, height, abdominal girth, and body composition) were collected via bioimpedance analysis (BIA) (BodyExplorer, Kommunikation & Service GmbH, Berliner Chaussee 74, 15234 Frankfurt, Oder). The blood was analyzed by the Wisplinghoff laboratory; parameters to determine postmenopausal status were estradiol, progesterone, and follicle stimulating hormone (FSH). To determine endurance capacity, a lactate threshold test was performed on a treadmill (Woodway PPS55med, Woodway GmbH, Steinackerstr. 20, 79576 Weil am Rhein): participants started at 5 km/h, and the speed was increased by 1.2 km/h every 5 min. Termination criteria for the test were reaching the maximal heart rate (220 minus age), feeling unwell or exhausted, or reaching 20 in the BORG scale. Hand-grip strength was tested via a grip test; to determine the maximal force for the chest via a chest press and leg strength via a leg press, the repetition maximum was tested according to Rühl [34]. According to Rühl, 1RM is calculated based on preformed repetitions.

All participants were randomly divided into an intervention group and a control group using a computer program (RITA version 1.51) while taking into account the parameters of age, weight, and walking speed (km/h) at 60% of the 4 mmol lactate/threshold. Before randomization, participants were stratified by age (<55, 55–60, >60 years old), by weight (<70, 70–90, >90 kg), and walking speed (km/h) at 60% of the 4 mmol/threshold (<4, 4–5, >5 km/h).

2.1.3. Training Intervention

Each woman received an individual parameter for endurance training. Over 3 weeks, for familiarization, walking training took place at a speed corresponding to 60% of the 4 mmol lactate threshold. Walking speed and heart rate were monitored by using sports watch Polar Ignite for training supervision. Subsequently, training was increased to 70% km/h of the 4 mmol lactate threshold for the following 4 weeks. Then, for the last 5 weeks, the training was at 75% km/h of the 4 mmol lactate threshold. All data were stored in the Polar Coach and tracked by the study management. Online strength training was offered twice a week via Cisco Webex Meetings (Cisco Systems GmbH). An alternate appointment was offered if participants were absent. The intervention and control groups completed the strength training together. All participants had to attend 80% of endurance training and 100% of strength training. Strength training consisted of bodyweight exercises such as squats, crunches, dips, and planks for all major muscle groups, such as M. quadriceps femoris, M. ischiocrurales, Mm. pectorales, M. triceps brachii, M. biceps brachii, Mm. glutei, and the trunk muscles. The gluteal and abdominal muscles must be constantly tensed to keep the body tense. The first 4 weeks were used for familiarization and a successive increase in intensity. Thus, we started with 10 repetitions in 3 sets, and increased to 12 repetitions in 3 sets. This was followed by an increase to 10 to 12 repetitions in 4 sets in the following 3 weeks. In the 8th week, a load–relief phase was scheduled with 8–10 repetitions in 4 sets before increasing to 12–15 repetitions in 4 sets in the last 4 weeks. In addition, the intensity of the exercises was increased through changes in execution. Each training session was organized as circuit training, so the strained muscle groups were changed and had time to relax. The cardiovascular system, however, was constantly strained. During the 12 weeks of the intervention, the women were not allowed to participate in other kind of sports (Figure 2).

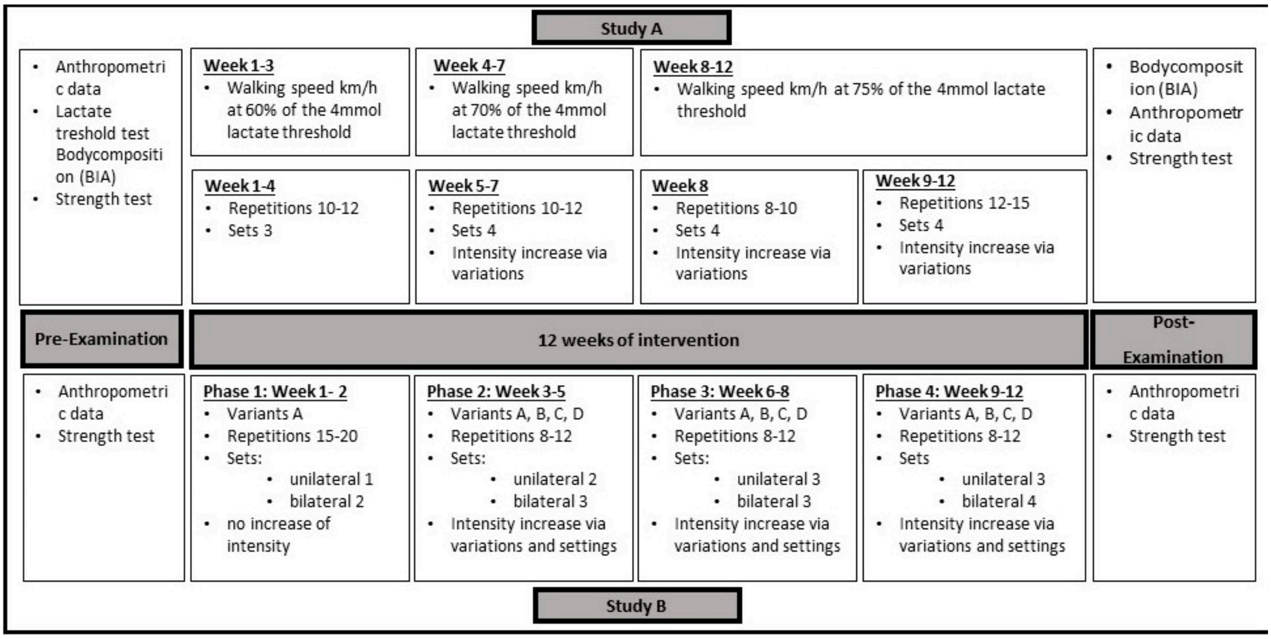

Figure 2. Study A and B protocols. Variants A–D describe the increase in difficulty by reducing the support base in each exercise variation.

2.1.4. Nutritional Intervention

The intervention group received protein/carbohydrate supplementation consisting of 100 g of sour milk cheese (Käserei Loose) and 76 g of white bread immediately after each training session. The nutritional values of the meal were 36.1 g protein, 35.3 g carbohydrate, 3.5 g fat, and 321 kcal. Sour milk cheese was provided by Käserei Loose, Leppersdorf, Germany (Table 1).

Table 1. Nutritional values in Studies A and B.

Study A	100 g Sour Milk Cheese and 76 g White Bread
Protein (g)	36.1
carbohydrate (g)	35.3
fat (g)	3.5
kcal	321
Study B	**100 g Sour Milk Cheese and 76 g White Bread and 250 mL Buttermilk**
Protein (g)	44.6
carbohydrate (g)	45.8
fat (g)	5
kcal	416

2.2. Study B: Effect of Sling Training and Protein/Carbohydrate Supplementation in Elderly Men and Women

2.2.1. Study Design and Participants

The study was designed as a randomized intervention study with two parallel groups (IG and CG). We included 35 participants in the randomization (Figure 3). Simple randomization was used, and care was taken to ensure an equal distribution ofparticipants. Stratification based on gender, age and weight data was performed during randomization. The sample size was determined on the basis of preliminary studies and the results of Gaedtke (2014). All participants completed sling training based on Gaedtke [35–37]. All men and women were recruited in the Ruhr area. Inclusion criteria were an age above 60 years and having been active in sports for at least one year. Exclusion criteria were an acute disease of the musculoskeletal system, cardiovascular diseases, and experience with sling training. After the study procedure had been communicated via telephone, and the inclusion and exclusion criteria had been checked, the interested participants received all information in paper form. Subsequently, an appointment was booked to sign the informed consent form, clarify existing questions, and start with the examinations. Prior to recruitment, the approval of the ethics committee of the German Sport University, Cologne (number 82/2015) was obtained. The study protocol was in accordance with the Declaration of Helsinki. The examinations and training sessions took place in a training center for seniors in Essen-Bochold and Gelsenkirchen-Mitte.

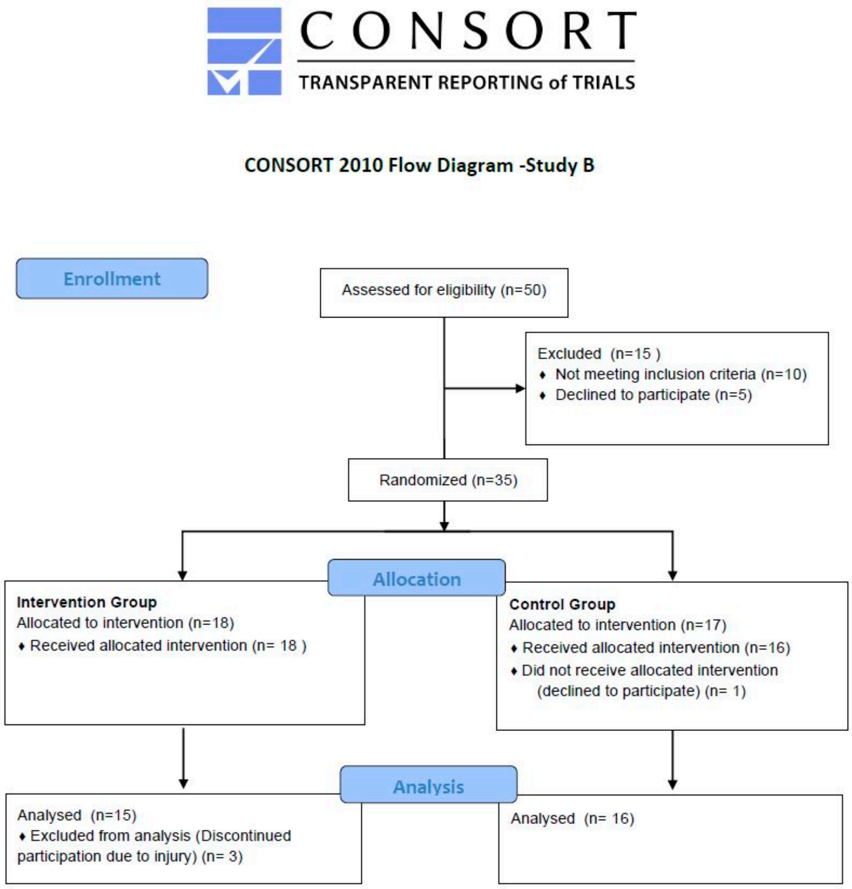

Figure 3. Consort flow diagram—Study B.

2.2.2. Test Day

The maximal force for chest (chest press) and leg (leg press) strength was established via the repetition maximum according to Rühl [34,38]. The Swiss Olympic trunk test was also performed for the ventral, dorsal, and lateral trunk muscles. The following program was followed according to Tschopp [39,40].

After a 10 min warm-up, ventral, lateral, and dorsal trunk strength was tested. The participants always had a 10 min break between individual tests.

Ventral trunk strength: From a plank position, feet were lifted alternately while contact had to be maintained with a control bar on the head and glutes. The time for which the correct position could be maintained was measured.

Lateral trunk test: From lateral support, the pelvis was lowered and raised again, and contact with the control bar on the pelvis had to be repeatedly established. The seconds were counted.

Dorsal trunk test: From a prone position on a box, the upper body was lowered and raised again, and the control bars had to be touched. The seconds were counted.

2.2.3. Training Intervention

The only training during the 12 weeks of intervention was sling training. Training took place three times per week (Monday, Wednesday, and Friday) and lasted 30 min. The whole group was divided into smaller groups of 3 to 6 to create a safe training situation. The intervention and control groups completed the training together. The training was divided into 4 training phases of 2 weeks. In the first phase of training, the participants were familiarized with the equipment, and the workout took place, so low intensity and high repetitions were used. Training control was performed with four different variations of an exercise (A–D), where A represented the easiest and D the most challenging variation. In the different variants, the difficulty was increased by reducing the support base (principle of the support base) [37].

Each training session included 7 exercises with 90 s rest between each exercise. The exercises were divided into:

- Two exercises for the upper body (rowing and chest press).
- Two exercises for the legs (squat and hip abduction).
- Two exercises for the trunk (crunches and side bend).
- One exercise for the entire ventral chain (body stretching).

The sequence of exercises was chosen so that one muscle group was not used twice in succession. Body tension is the basis of every exercise. The gluteal and abdominal muscles must be constantly tensed to keep the body in extension. In addition, the shoulders always remain low, and the neck relaxed. These points were emphasized in each unit.

The number of repetitions Increased after a subject had achieved two more repetitions on one exercise in the last set over two training sessions (progressive overload). This ensured progression in the training, which started with 8 repetitions and ended with 12. Once the 12 repetitions had been reached, the intensity was increased using the OMNI Res value. For this purpose, the trainer asked for a value between 1 and 10 after each set, where 1 meant very low effort and 10 meant very high effort [41]. On the basis of the training goal, 6 and 8 was the optimal intensity range. Using the settings, the suspensions or variant intensity could be increased if the value was less than 6 or decreased if the value was greater than 8 (Figure 2).

2.2.4. Nutritional Intervention

After the training session, the intervention group received 100 g of sour milk cheese (Käserei Loose), 76 g of white bread, and 250 mL buttermilk immediately after each sling training session. The nutritional values of the meal were 44.6 g protein, 45.8 g carbohydrate, 5 g fat, and 416 kcal. Sour milk cheese and buttermilk were provided by Käserei Loose, Leppersdorf, Germany (Table 1). After each training session, all participants remained in the training center for 30 min to ensure that only the intervention group received the protein/carbohydrate supplementation.

2.3. Statistical Analysis

Strength data were normalized to body weight prior to further analysis. Subsequently, they were processed with principal component analysis (PCA). All variables had been mean centered and scaled to unity variance. The total variances of the datasets thus amounted to 4.0 (Study A) and 6.0 (Study B). PCA was performed on the data acquired before the intervention periods. Postintervention data then were submitted to PCA transformation using previously obtained coefficients. This procedure facilitated the detection of possible changes in the latent variables represented by the strength dataset.

The variables extracted with PCA were then analyzed with linear mixed-effect models (LME). As we were interested in the experimental effects of training intervention combined with supplementation, the fixed effects consistently encompassed these factors and their corresponding interaction term.

For Study B, the subjects were classified according to their adiposity status (BMI > 30). Adiposity served as an additional covariate with two levels (adipose: Adip+, not adipose: Adip−). Because participants in Study B were significantly more overweight and also obese compared to participants in Study A, we decided to analyze weight as a covariate. In addition, the interaction of adiposity and training intervention was included. The incorporation of higher-order interaction terms was not feasible due to the restricted sample size. Time (i.e., training intervention) grouped within individuals consistently served as a random effect. The used software was the latest version of statistical language R [42]. LMEs were fitted with the use of R's standard nlme library [43]. The assessors were not blinded, but the data analysis staff were blinded in both studies.

3. Results

3.1. Study A

A total of 51 postmenopausal women (57.3 ± 3.0 years) finished the study (Table 2). Reasons for dropouts were diseases/injuries (N = 4), elevated hormone levels that did not meet the inclusion criteria (N = 4), and too much time expenditure (N = 4). None of the diseases or injuries were related to training.

Table 2. Anthropometric data with mean and standard deviation—Study A.

	Total Sample	Intervention Group	Control Group
Study A	N = 51	N = 24	N = 28
Age (years)	57.3 ± 3.0	57.9 ± 3.3	56.8 ± 2.8
Height (cm)	167 ± 7.3	169.8 ± 6.9	164.6 ± 6.7
Weight (kg)	69.7 ± 12.7	70.8 ± 15.2	68.8 ± 10.3
BMI	25.1 ± 4.4	24.5 ± 4.7	25.5 ± 4.2

Table 3 shows the changes in the strength and body composition of the intervention and control groups; all strength parameters could be increased. PCA showed that the individual strength parameters could be represented as a general strength score. There was a significant training effect, but the effect of the influence of supplementation was not significant. A change in body composition with a reduction in fat and an increase in muscle mass was also evident.

Table 3. Strength parameters and body composition showing the mean and standard deviation—Study A.

N = 51	Intervention Group		Control Group	
	Pre Intervention	Post Intervention	Pre Intervention	Post Intervention
Strength				
Leg (kg)	89.9 ± 20.9	95.9 ± 24.2	91.4 ± 26.4	105.0 ± 25.9
Chest (kg)	28.0 ± 8.2	31.9 ± 8.4	25.5 ± 5.6	27.7 ± 5.7
Hand-grip right (kg)	28.9 ± 4.7	31.3 ± 4.0	27.8 ± 4.2	29.0 ± 3.9
Hand-grip left (kg)	27.9 ± 4.5	29.1 ± 3.9	26.8 ± 4.5	27.5 ± 4.3
Hand-grip sum (kg)	51.1 ± 18.9	54.2 ± 18.9	53.5 ± 9.4	56.5 ± 7.6
Body composition				
Body weight	70.8 ± 15.2	70.5 ± 15.5	68.8 ± 10.5	68.1 ± 10.1
Muscle mass	19.1 ± 2.4	19.3 ± 2.5	18.8 ± 1.8	19.2 ± 2.0
Fat mass	25.6 ± 11.0	25.2 ± 11.1	24.4 ± 7.7	23.4 ± 7.1

3.1.1. PCA

The PCA yielded merely one significant component, i.e., one variable with variance larger than unity (PC1) that contained 0.65% of the total variance. Therefore, all four strength values (chest strength, leg strength, and left- and right-hand-grip strength) were combined into one strength value, the general strength score (GS).

3.1.2. LME

Figure 4 shows the changes in general Strength score (intervention group = Treat; control group = Ctrl). Table 4 shows the significant changes due to training. Training intervention had a positive and strongly significant effect o (+0.65, $p \leq 0.001$) but supplementation had no detectable additional effect (ca. 0, p = ca. 0.85). Figure 4 shows significant increases in general strength.

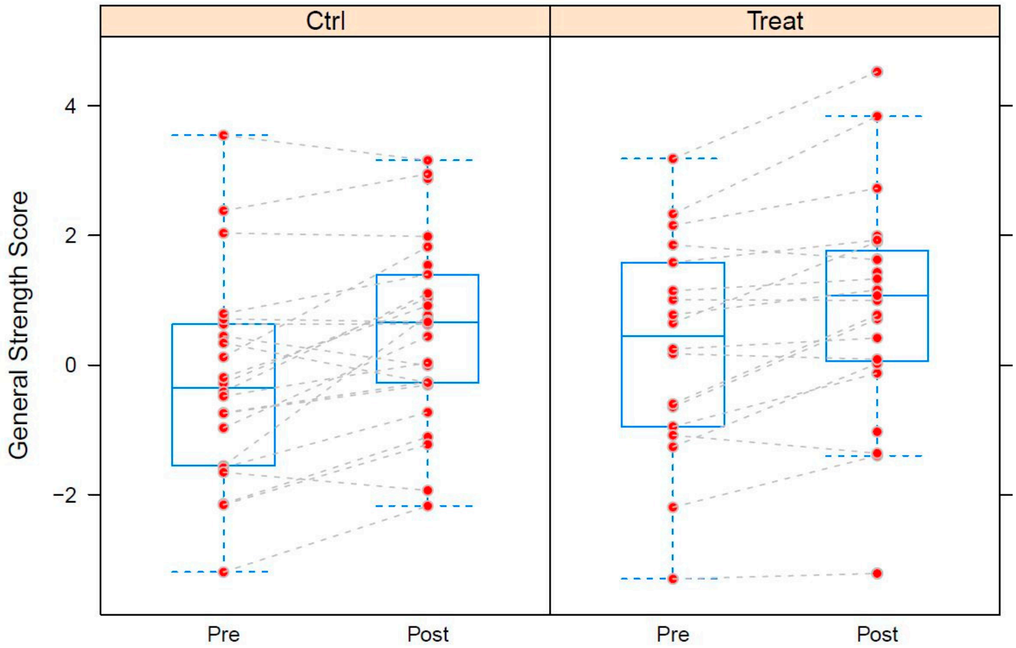

Figure 4. Box-plots of the General Strength Score (GS) calculated from the strength data of study A grouped by supplementation (Ctrl: control group; Treat: treatment group). Pre: measurement before training intervention; Post: measurements after training intervention. GS corresponds to the 1st principal component extracted from the strength data. See text for detailed explanation of the score. The box-plots indicate minima, 1st quartiles, medians, second quartiles and maxima, respectively. Maxima or minima falling beyond the median ± 1.5 times the respective interquartile range ("outliers") are placed outside the whiskers. Dashed lines correspond to repeated measurements of the same subjects.

Table 4. LME parameters fitted to GS data.

	Value	Std. Error	DF	t-Value	*p*-Value
(Intercept)	−0.0888	0.321	46	−0.276	0.784
TimePost	0.649	0.15	38	4.32	0.000108
GrpTreat	0.398	0.467	46	0.851	0.399
TreatPost × GrpTreat	−0.0427	0.224	38	−0.191	0.85

3.2. Study B

A total of 31 participants comprising 6 men and 25 women finished the study (65.9 ± 4.9 years) (Table 5). We excluded 3 participants during the 12 weeks because of injuries. None of the diseases or injuries were related to training.

Table 5. Anthropometric data showing mean and standard deviation—Study B.

	Total Sample	Intervention Group	Control Group
Study B	N = 31	N = 15	N = 16
Age (years)	65.9 ± 4.9	67.7 ± 5.9	64.2 ± 3.2
Height (cm)	166.1 ± 8.5	165.3 ± 9.2	166.9 ± 7.9
Weight (kg)	85.4 ± 15.6	87.3 ± 14.9	83.6 ± 15.5
BMI	30.9 ± 5.1	31.8 ± 4.1	30.0 ± 5.7

3.2.1. PCA

Table 6 shows strength increase and body-weight decrease values. All participants gained strength and lost body weight. Using PCA, two strength scores (limb strength and trunk strength) could be formed from the six strength values (leg, chest, ventral-trunk, dorsal-trunk, and left and right lateral-trunk strength). PCA yielded two significant components, PC1 and PC2, with 0.55% and 0.25% of the total variance, respectively. Thus, the cumulative variance amounted to 80%.

Table 6. Changes in the strength and body weight of control and intervention groups with the mean and standard deviation.

N = 31	Intervention Group		Control Group	
	Preintervention	Postintervention	Preintervention	Postintervention
Leg strength (kg)	117.0 ± 41.7	142.9 ± 50.2	105.3 ± 32.2	130.8 ± 32.3
Chest strength (kg)	39.7 ± 14.8	46.5 ± 15.9	30.4 ± 26.2	44.9 ± 30.8
Ventral-trunk strength (sec)	30.3 ± 18.1	49.4 ± 21.1	27.8 ± 4.2	29.0 ± 3.9
Lateral-trunk strength—right	12.9 ± 11.7	30.6 ± 16.2	12.4 ± 11.4	19.8 ± 13.9
Lateral-trunk strength—left	19.4 ± 13.5	30.7 ± 13.0	13.1 ± 9.3	21.8 ± 12.4
Dorsal-trunk strength	65.2 ± 41.3	79.6 ± 49.8	62.5 ± 26.4	85.6 ± 31.7
Body weight	87.2 ± 14.9	85.7 ± 14.3	83.6 ± 15.4	82.6 ± 15.2

3.2.2. LME

Tables 7 and 8 show the parameters of the LMEs fitted to trunk-strength (TS) and limb-strength (LS) data, respectively. TS significantly increased during the training intervention (+2.305, $p \leq 0.001$). While adipose subjects exhibited lower starting values (−1.683, $p \leq 0.05$), they also react significantly more weakly to the training intervention (−1.513, $p \leq 0.01$). Dietary supplementation yielded an additional and significant positive effect on TS (+0.950, $p \leq 0.05$) (Table 7 and Figure 5). LS significantly increased after the training intervention (+0.753, $p < 0.05$). Apart from a weak initial trend of adipose subjects showing stronger values (+0.942, $p = 0.096$), there were no further significant terms in the model (Table 8 and Figure 6).

Table 7. LME parameters fitted to the trunk strength score (PC1, TS) of Study B.

	Value	Std. Error	DF	t-Value	*p*-Value
(Intercept)	0.157	0.551	25	0.285	0.778
TimePost	2.305	0.291	19	7.921	0.000
AdipAdip+	−1.683	0.763	25	−2.207	0.037
GrpTreat	0.856	0.758	25	1.130	0.269
TimePost × AdipAdip+	−1.513	0.407	19	−3.718	0.001
TimePost × GrpTreat	0.950	0.407	19	2.331	0.031

Table 8. LME parameters fitted to the limb-strength score (PC2, LS) of Study B.

	Value	Std. Error	DF	t-Value	*p*-Value
(Intercept)	−0.247	0.393	25	−0.628	0.536
TimePost	0.753	0.274	19	2.751	0.013
AdipAdip+	0.942	0.545	25	1.728	0.096
GrpTreat	−0.562	0.543	25	−1.034	0.311
TimePost × AdipAdip+	−0.364	0.383	19	−0.952	0.353
TimePost × GrpTreat	−0.352	0.383	19	−0.917	0.371

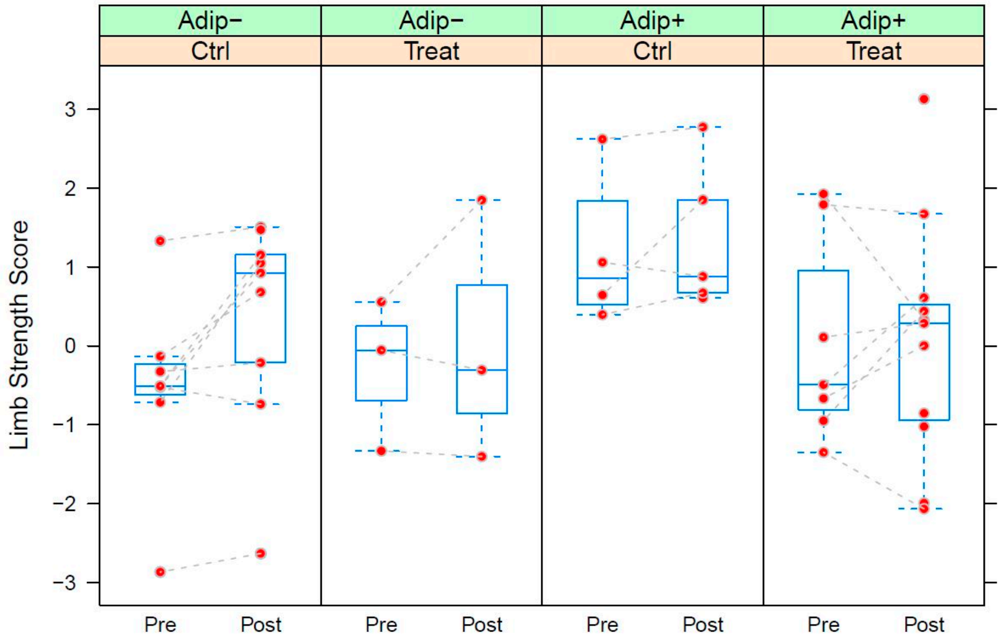

Figure 5. Box-plots of the Limb Strength Score (LS) calculated from the strength data of study B grouped by supplementation (Ctrl: control group; Treat: treatment group) within adiposity status (Adip−: BMI <30, Adip+: BMI >= 30). Pre: measurement before training intervention; Post: measurements after training intervention. LS corresponds to the 2nd principal component extracted from the strength data. See text for detailed explanation of the score. See capation of Figure 4 for details of the box-plots.

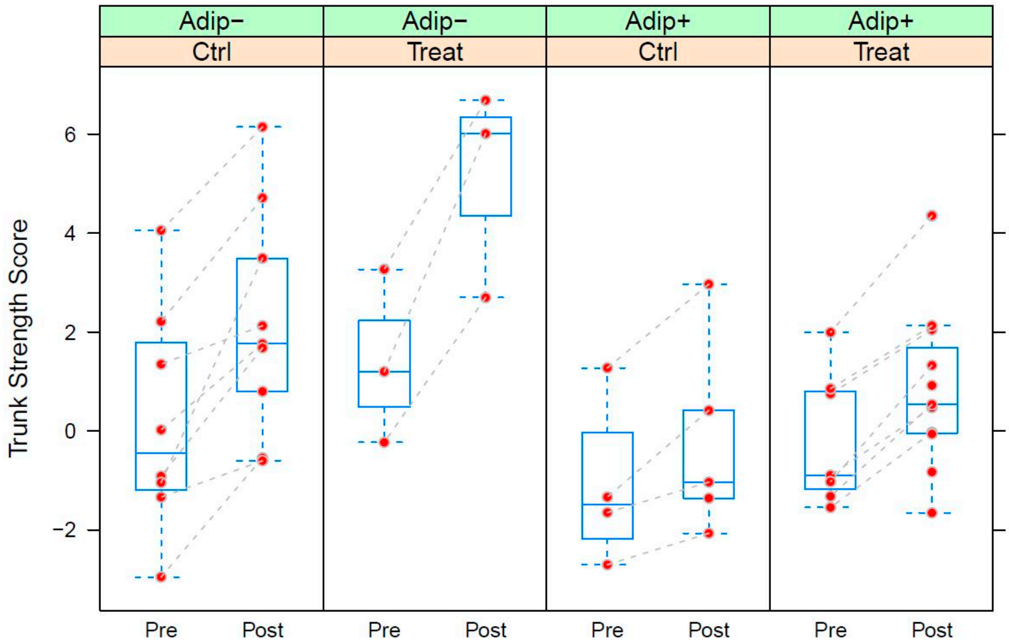

Figure 6. Box-plots of the Trunk Strength Score (TS) calculated from the strength data of study B grouped by supplementation (Ctrl: control group; Treat: treatment group) within adiposity status (Adip−: BMI < 30, Adip+: BMI >= 30). Pre: measurement before training intervention; Post: measurements after training intervention. TS corresponds to the 1st principal component extracted from the strength data. See text for detailed explanation of the score. See caption of Figure 4 for details of the box-plots.

4. Discussion

We compared two different training types in combination with protein/carbohydrate supplementation via food immediately after training in postmenopausal women, and elderly men and women. Both studies showed a positive effect of training; sling training increased limb and especially trunk strength in elderly men and women. Gaedtke showed significant results on chest-muscle strength in elderly people through sling training [35]. Various studies showed a positive effect of sling training on muscle mass in general and the trunk muscles in particular [36,44–47]. Trunk-muscle strength was more promoted in the IG after the consumption of sour milk cheese, bread, and buttermilk than that in the CG. We were not able to show this effect in limb strength. However, training was significantly more effective in the intervention group. Sling training is common as a treatment for lower-back pain, which is often triggered by a deficit in the trunk muscles. Local trunk muscles are a possible explanation for the larger effects in trunk strength [48,49]. Protein/carbohydrate supplementation seemed to be able to intensify these positive effects (Figure 5), perhaps due to the proregenerative effects that Isenmann and colleagues described [27]. The elderly participants regularly use their leg and chest muscles in everyday life, so the proregenerative effects could not show a large effect. However, as aging trunk muscles slim down, sling training with a focus on trunk stabilization, like our training, is a great challenge and requires these muscles. The training was offered three times per week. Therefore, there may be proregenerative effects, such as an increase in insulin serum concentration, a decrease in proinflammatory markers, and an increase in anti-inflammatory markers. Isenmann and colleagues showed these effects in young men after a similar protein/carbohydrate supplementation via food immediately after training [27]. The positive proregenerative effect of protein/carbohydrate supplementation after training was also shown by other authors [26,50]. Zawadzki and colleagues showed that the administration of a protein/carbohydrate combination right after training could enhance glycogen storage in muscles, which contributes to faster recovery. Leg and chest strength also increased over the 3 months, but this effect was not increased via protein/carbohydrate intake [50].

The significant training effect was less pronounced in participants with a higher BMI (>30) than that in participants with a lower BMI (Figures 5 and 6). A possible explanation could be that, with greater body weight, the sling exercises could not be performed as well or could only in simpler variations, which could have caused a reduced training effect. Morat et al. showed that variations in body angle while training intensify the sling training [47]. On the other hand, the participant group was more likely to have the high body fat percentage that caused the high BMI. Since untrained and overweight individuals usually experience faster and greater effects with the same training than those of persons with normal weight, such effects were also more likely here [51]. Therefore, it is reasonable to assume that sling training was not as effective for heavier participants. In summary, a significant increase in strength was achieved in the seniors as a result of the training, which is a very positive effect, especially with regard to the risk of sarcopenia. Supplementation with food in the form of an evening meal increased trunk strength more significantly, which is an important aspect with regard to frailty in old age.

The combination of endurance and strength training for postmenopausal women could increase strength and made the women feel more fit. We showed effects in whole body strength, which consists of chest, leg, and hand-grip strength. The effect on the hand grip is important for postmenopausal women because many of them have low bone and low muscle mass, which comes with a low hand grip. In addition, low hand-grip strength is associated with a low quality of life [52]. Using principal component analysis, we and other authors showed that hand-grip strength could be used as an indicator of overall body strength [53]. So, these findings are in line with the increase in and the role of hand-grip strength. Thus, the increase in hand-grip strength may explain the increase in the subjective fitness status of the participants. Leg and chest strength was analyzed via the repetition maximum, which is a possible reason for the lesser effects. In this repetition method, the one repetition maximum (1 RM) is not tested, but calculated on the basis of weight and repetitions. This method can be used especially for untrained and inexperienced people, and in medical training therapy [54]. In a heterogeneous group (experienced and inexperienced or trained and untrained participants), however, this can lead to errors or unequal results. We were not able to demonstrate a significant influence of supplementation even if hand strength increased more significantly.

In Study B, there was a significant decrease in body weight; in Study A, we were unable to show this. However, participants in Study A with a BMI of 25.1 were normal to slightly overweight compared to the participants in Study B (BMI 30.9). In addition, in Study B, strength training was performed 3 times per week, whereas in Study A, moderate and fat-metabolism-oriented endurance training was performed twice per week, and strength training only once per week. Thus, endurance training had an effective effect on fat mass, whereas strength training had a faster effect on body weight [5]. Here, the exact determination of body composition in Study B would have been helpful.

The limitations of our study are the missing analysis of insulin, skeletal-muscle creatine kinase, myoglobin, and serum cytokine levels in both studies that would have contributed to proving the proregenerative effect. Nutritional and protein statuses were not recorded before and during training in either study, which would have been useful in identifying possible deficiencies in the supply or oversupply of dietary protein, especially since the effect of protein/carbohydrate supplementation was so pronounced in older participants. One hypothesis here is that the postmenopausal women consume sufficient protein in their diet, while the seniors showed a deficit. In Study B, protein/carbohydrate supplementation was provided as a common meal in the evening after training: sour milk cheese, bread, and buttermilk. In Study A, this effect was absent because no communal meal was possible after training due to the COVID-19 pandemic. Thus, some participants trained in the morning and supplemented the protein/carbohydrate combination afterwards, and others trained in the evening. Due to the different training times, the supplementation was not taken together as a meal, which may have led to participants taking the supplementation in addition, while others replaced a meal with it. This could explain the missing change in body weight. The supervision of the consumption of sour milk cheese and bread after each training session was also lacking, which presumably reduced compliance among the women. In Study B, body composition was not determined, so conclusions could be drawn about the changes in body weight, but not about the exact body composition. These parameters would have been useful to see the influence of training and protein/carbohydrate intake on muscle and fat mass. Since the body weight of the subjects in Study B were significantly higher (85.4 ± 15.6 kg) than those in Study A (69.7 ± 12.7 kg), the exact body composition would have been an interesting parameter to compare baseline muscle and fat mass because a significantly lower baseline value would be assumed for the seniors, according to [17,55]. Study B also showed that the training effect was less pronounced in participants with a higher BMI (>30) than that in lighter participants. This may have been due to the nature of the training, as the participants' entire weight had to be carried on the slings. This is much more difficult with a greater body weight and may mean, for example, that the exercises could only be increased more slowly.

5. Conclusions

Our results indicated that a combination of training and protein/carbohydrate supplementation via food directly after training may be a suitable strategy to counteract the age-related loss of trunk strength in seniors. The combination of strength and endurance training in postmenopausal women, and sling training in older subjects led to improved strength. We only demonstrated the influence of protein/carbohydrate supplementation regarding specific parameters, but this may have been due to methodological limitations and the COVID-19 pandemic. In the future, body composition should be taken into account, and the meal character of protein/carbohydrate supplementation should be adhered to. In addition, it would be interesting to perform Study A with a group of participants with a BMI above 30.

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Institutional Review Board Statement: The studies were conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of German Sports University, Cologne Study A (number 008/2021; date of approval 25.1.2021) Study B (82/2015 and date of approval).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

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Serum Stable Calcium Isotopes ($^{44}Ca/^{42}Ca$) indicate beneficial Effects of moderate Training on Bone Metabolism in postmenopausal Women

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Abstract

Objective

Assessment of potentially beneficial effects of moderate strength training on bone health in postmenopausal females. Serum $\delta^{44/42}Ca$-ratios served as biomarker for bone metabolism.

Study Design

Randomized trial, $n = 51$ postmenopausal underwent a 12 week training intervention. Intervention given by endurance training (walking, 2/w) and bodyweight training 1/w. Randomized sub-sample ($n = 26$) submitted to calcium isotope analysis.

Main outcome measures

Serum stable calcium isotope ratios ($^{44}Ca/^{42}Ca$ by ICP-MC-IRMS), leg strength (leg press), chest strength (bench press), handgrip strength (dynamometer), daily step equivalents (wearable tracker), body composition (BIA). All measures registered before and after intervention interval.

Results

Population serum $\delta^{44/42}Ca$-values increased by 0.057 ‰ ($p < 0.001$, LME). Individual intercepts and changes correlated significantly ($\rho = -0.52$, $p < 0.05$, LME likelihood statistics). No significant effects of any covariate could be detected.

Conclusions

Moderate, health-oriented strength staining may significantly improve bone metabolism in postmenopausal women. Beneficial effects are more pronounced in subjects with more adverse bone metabolism.

Key Words

Bone Metabolism, Calcium Stable Isotopes, Osteoporosis, Exercise, Menopause.

Introduction

As of 2021, roughly 18 % of the world population suffered from osteoporosis [1]. The burden of disease is enormous and osteoporosis still exhibits rising prevalence [2]. The incidence strongly increases with age [3]. Consistently, females exhibit higher prevalences and incidences [1,3]. In Germany, as compared to males, the prevalence is two times higher. It generally increases up to fourfold per decade beyond ages > 50 y [4]. This is usually attributed to concomittant estrogen deficiency [5]. In Germany, up to one third of elderly females develop osteoporosis. Pathogenesis studies suggest predominant bone mass losses during perimenopause [6] and within few years after menopause onset [7,8]. Sufficient amounts of physical exercise appear outstandingly relevant to osteoporosis prevention. Additional to micronutrient supply and to refraining from alcohol and nicotine, regular exercise is advantageous to bone health [5,9,10]. Corresponding recommendations cover a plethora of practices [11–13]. The prospective assessment of exercise amounts beneficial to bone metabolic balance (BMB) proves difficult. Specifically, conventional bone mineral density (BMD) measurement by dual energy x-ray absorptiometry (DXA) features significant methodological issues [14]. Firstly, this biomarker reacts only slowly. Then, repeated exposition of healthy subjects to radiation is ethically problematical. But most importantly, DXA merely is applied to preselected skeletal locations.

Eisenhauer *et al.* suggest $^{44}Ca/^{42}Ca$ analysis in blood and urine to assess BMB [14]. The method features excellent diagnostic validity. It exploits physiological Ca isotope fractionation during bone mineralization [15]. Notably, $^{44}Ca/^{42}Ca$ ratios integrate gross bone metabolism. The procedure is hence advisable for physiological experiments on systemic scales. It favorably also lacks radiation exposure which renders it uncritical for longitudinal studies.

In terms of practical considerations there is yet another important issue: Steady compliance to exercise regimens generally presupposes attractive low-threshold opportunities. Broad combinations of moderate drills are therefore preferable. The demands of injury prophylaxis and of cardiovascular health also favor this concept. However, physiologically, this implies rather non-specific and locally fuzzy stimulation of bone metabolism. Nonetheless, corresponding adaptations are presumably quite beneficial.

In the present study we will try to detect systemic improvements of BMB induced by moderate health-oriented training. To this end, serum $^{44}Ca/^{42}Ca$ constitutes an outstandingly suitable biomarker from our point of view.

Methods

General

Practical examinations were conducted at the German Sport University Cologne (DSHS). The study was performed between 1/2021 and 11/2021. The effective protection measures concerning the COVID-19 pandemic were strictly followed. Ethical approval was obtained prior to recruitment (DSHS, 008/2021). Compliance with the Declaration of Helsinki was a coercive preequisite. The study was registered in the German Clinical Trials Register (DRKS-ID DRKS00024144). All subjects signed written informed consent to the study.

Subjects

Postmenopausal women (50 to 65 y) were recruited. The primary inclusion criteria was demonstrable postmenopausal status, *i. e.* that menses lastly occurred more than two years ago. Serum 17β-estradiol (E2) had to fall below 32 pg/ml. FSH had to fall between 31.6 to 116.3 mIU/ml.

Exclusion criteria were any kind of exercise limiting diseases (endocrinological, neurological, muscular, gastrointestinal). Cancer histories (5 y), specifically unbalanced diets (*e. g.* vegan), smoking, and hormone substitutions. The subjects exercised at most twice a week habitually.

$^{44}Ca/^{42}Ca$ analyses eventually were performed on a randomized subset (n = 26) from a larger population. See Hofmann *et al.* [16] (study A) for details.

Exercise

The training encompassed endurance training (2/w) and body weight strength training (1/w). Self-reliant endurance training was monitored by wearables ("Polar Ignite", "Polar Coach" software, Polar Electro GmbH, Büttelborn, Germany). Specifically, walking speed and heart rates were tracked.

Following familiarization (3 w) at walking speeds corresponding to 60 % of the 4 mmol lactate threshold (4LT), 4 weeks were trained at speeds corresponding to 70 % 4LT. Another 5 weeks corresponding to 75 % 4LT then followed up.

Due to COVID-19 induced restrictions, instructed strength training was performed online (Webex Meetings, Cisco Systems GmbH, Garching, Germany).

Strength training covered all main muscle groups. The sessions were organized as circuit training and encompassed 8 well-proven functional drills, respectively. [1] Table 1 shows the workloads and the periodization. A familiarization interval without significant workloads (4 w) preceded the intervention. Strained and rested muscle groups alternated systematically. Yet, the cardiovascular system was constantly engaged. Where appropriate, exercise intensities were adapted by instructed changes in execution.

Table 1: Workloads and periodization of the body weight strength training.

Week	No. of Drills	Reps. per Drill	Sets	Total No. of Reps.
1-4	8	10	3	240
5-7	8	12	3	288
8	8	8-12	4	*ca.* 320
9-12	8	12-15	4	*ca.* 430

Categorically, the participants had to complete 80 % of the endurance volume and 100 % of the strength volume. Poorer compliance resulted in exclusion. In case of hindrances, alternative dates were offered in order to avoid dropouts. The subjects were to refrain from all other sports during the intervention interval.

Blood Sampling, Anthropometric Data and Functional Variables

The subjects reported to the laboratory in fasted state (last ingestion > 12 h before). After collection of blood samples anthropometric data were measured: body mass [kg] (BM), height [cm], abdominal girth [cm].

Endurance capacities were determined by lactate threshold on a treadmill (Woodway PPS55med, Woodway GmbH, Weil am Rhein, Germany). The initial speed was 5 km/h incremented by 1.2 km/h each 5 min.

Termination criteria for the test were as follows:

Theoretical maximum heart rate ($220 \times min^{-1}$ - age [y])

Subjective exhaustion

Strain level 20 (Borg-scale)

Right and left hand grip strengths (GSR and GSL, respectively) were measured by hand-held dynamometer (Jamar Digital Plus, PhysioSupplies, Biederitz, Germany).

Strength performances for bench press (BP1RM) and leg extension (LP1RM) were assessed *via* the repetition method. Maximum strengths were estimated according to Rühl and Schuba [17]. After thorough warm up, one set was passed until failure. Appropriate rest periods were met, respectively. Conventional strength training machines were employed (bench press and leg press, GYM80 International, Gelsenkirchen, Germany).

Body Composition

Body composition was analyzed by bio-impedance-analysis (BIA, BodyExplorer 2006, Kommunikation & Service GmbH, Frankfurt/Oder, Germany). BIA measurements yielded total body water (TBW), muscle mass (SM), fat mass (FM), and for lean body mass (LBM).

Calcium Stable Isotope Analysis

Calcium isotope ratios of serum samples were analyzed by multiple collector inductively coupled plasma mass spectrometry (MC-ICP-MS) at the GEOMAR Helmholtz Center for Ocean Research Kiel, Germany. Eisenhauer *et al.* [14] provide the methodology. $^{44}Ca/^{42}Ca$ ratios are expressed relative to a standard (STD). The standard material is NIST SRM 915a ($CaCO_3$) [18]. Differences of $^{44}Ca/^{42}Ca$ between sample and STD are calculated

[1] A detailed list of drills, including precise exercise and rest intervals is available from the authors.

according to the δ-notation: $\delta^{44/42}Ca = [(R_{SPL}) / R_{STD}) - 1] \times 10^3$, where R_{SPL} and R_{STD} correspond to the $^{44/42}Ca$ ratios of sample and standard, respectively. Subtraction of 1 zeroes the δ-value of R_{STD}. Multiplication by 10^3 removes insignificant digits and effects use of “per mil” (‰) as (pseudo-)unit for $\delta^{44/42}Ca$.

Data Analysis

Functional data, *i. e.* BP1RM, LP1RM, GSL, and GSR at T_0 were combined by principal components analysis (PCA). PCA then was projected on T_1. The first principal component (“F-score”) subsequently served as covariate. The identical procedure was applied to BIA and anthropometric data (TBW, SM, FM, LBM, BMI, BM, AG). The first principal component (“BC-score”) again served as covariate. Both scores originally were derived from a larger super-set [16].

Potential effects on the $^{44}Ca/^{42}Ca$ ratios were analyzed by linear mixed effects models (LME) [19]. Serum $\delta^{44/42}Ca$ consistently represented the dependent variable. Time (T_0, T_1) always constituted the primary covariate (fixed effect). Potential secondary covariates were step-wise included and tested against simpler models.

Individual $^{44}Ca/^{42}Ca$ intercepts and slopes served as random effects. Initially, zero correlation between these effects was enforced. A second model allowed for correlation. See Pinheiro and Bates [19] for details.

Different models were compared by likelihood statistics and by Akaike’s information criterion (AIC) [20]. Data analysis was performed by the R statistical language [21]. R’s nlme-library was required for LME fitting [22].

Results

Table 2 shows the anthropometric data of the subjects that completed the study.

Table 2: Anthropometric data of the investigated subjects (means ± standard deviations).

n	Age [y]	Height [cm]	Mass [kg]	BMI [kg × m^{-2}]
26	57.0 ± 2.7	169 ± 6.8	69.9 ± 13.3	24.5 ± 4.2

Four subjects dropped out due to disease, injuries, or personal reasons.

The F-score represents *ca.* 65 % of the total variance of the strength data where the measured variables contribute to varying degrees. Table 3 shows the loadings.

Table 3: Loadings of PC-1 extracted from the strength data by PCA (F-Score). See text for details.

LP1RM	BP1RM	HSL	HSR
0.335	0.47	0.595	0.559

The BC-Score represents more than 90 % of the total variance of BIA data combined to anthropometry. All variables contribute to comparable degrees, if at different signs. Table 4 shows the loadings. Higher BC-scores inidicate larger fat but lower muscle proportions.

Table 4: Loadings of PC-1 extracted from the anthropometric data and from the BIA measurements by PCA (BC-Score). See text for details.

FM	SM	TBW	LBM	BMI	BM	AG
0.391	-0.373	-0.391	-0.391	0.362	0.367	0.368

Table 5 shows the changes of the F-scores and of the BC-scores. There is a statistically significant increase of the general strength following the intervention. Body compositions, by contrast, do not change significantly.

Table 5: Paired t-tests of the two scores calculated from the strength data and from the BIA data of the population. Higher F-Scores indicate larger general strength values; higher BC-Scores larger proportions of body fat at lower proportions of muscle mass. See text for details.

Variable	Difference	*t* value	DF	*p*
F-Score	+0.775	4.954	17	< 0.001
BC-Score	-0.218	-1.114	20	0.278

Figure 1 shows the serum $\delta^{44/42}$Ca values before (T_0) and after (T_1) the training intervention. The medians amount to -0.950 ‰ and -0.895 ‰, respectively.

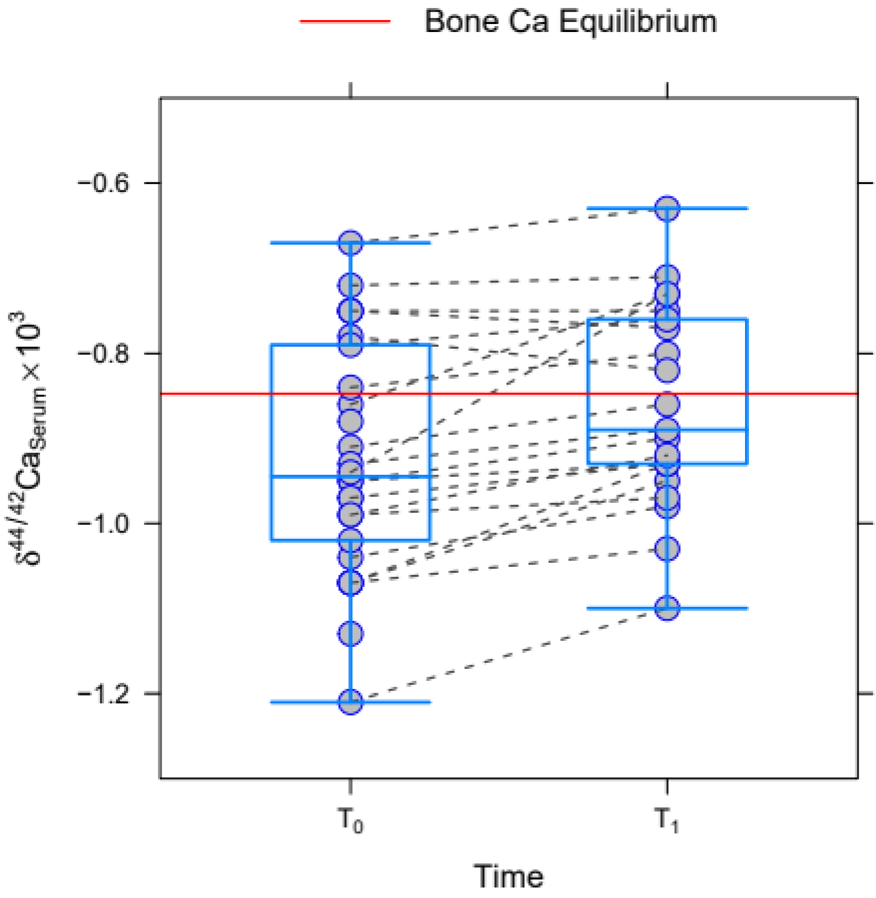

Figure 1: Serum $\delta^{44/42}$Ca in postmenopausal women before (T_0) and after (T_1) training intervention. The horizontal line indicates bone metabolic equilibrium ($\delta^{44/42}$Ca = -0.8475 ‰).

The model with correlated random effects fitted significantly better than that featuring enforced zero correlation ($p < 0.05$, likelihood ratio 4.6). AIC dropped from -86.8 to -89.4. The corresponding correlation coefficient was -0.51. Hence, lower intercepts are statistically associated with stronger increases of ^{44}Ca/^{42}Ca. Figure 2 shows the scatter-plot. The empirical correlation (ρ = -0.52) of both measures is virtually identical to the LME estimate.

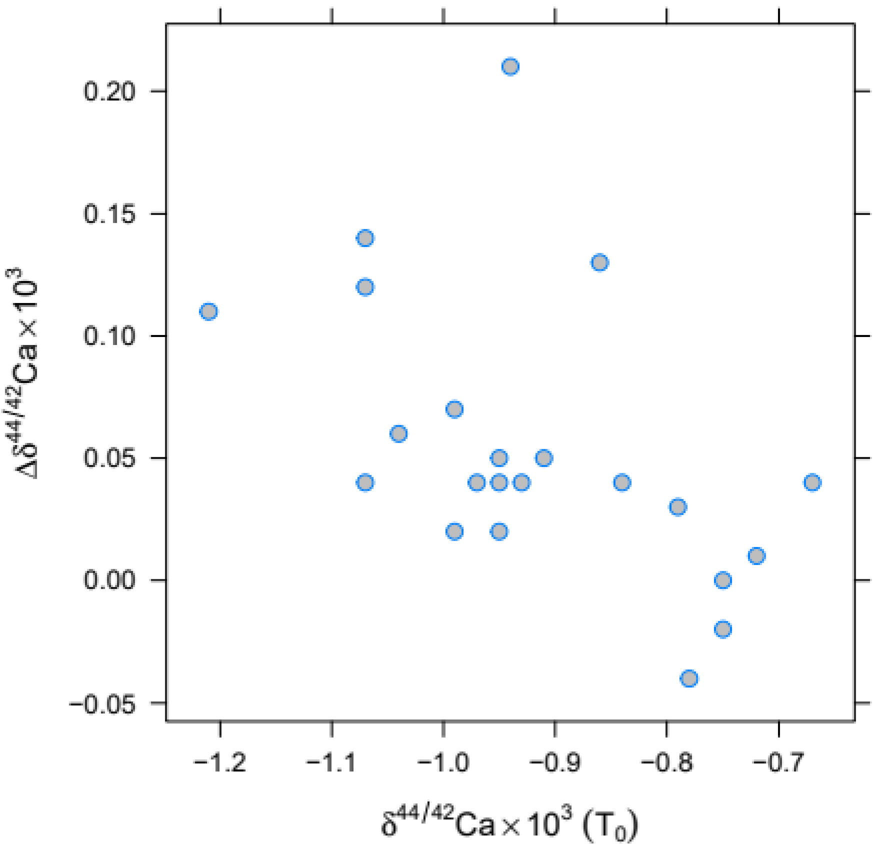

Figure 2: Random effects correlation (intercepts, slopes) of the LME fitted to $\delta^{44/42}$Ca values.

None of the covariates (age, F-scores, BC-scores, step equivalents) caused significant improvements of the LME-fits. Neither first nor second order polynomials of the covariates nor corresponding interactions with time tested significant. AIC consistently worsened upon inclusion of any covariate.

Table 6 shows the fixed effects of the LME. Following intervention (T_1) the $\delta^{44/42}$Ca values increase highly significant.

Table 6: Fixed effects of the linear mixed effects model fitted to the $\delta^{44/42}$Ca values.

	Value	Std.Error	DF	*t* value	*p*
Intercept	-0.927	0.024	28	-38.03	
Time T_1	0.057	0.012	22	4.85	< 0.001

Discussion

The average $\delta^{44/42}$Ca value was -0.927±0.024 ‰ before intervention (LME estimate ± std. error). This is well below the metabolic equilibrium equivalent of -0.85 ‰ [14]. The increase by 0.057±0.012 ‰ does not indicate complete cushion of catabolism. But it undoubtfully represents a major improvement. Furthermore, the moderate training regimen was generally attractive to the subjects. The compliance was excellent while drop-outs were negligible. Some subjects may adapt lifestyles accordingly. The design employed leisure sports activity rather than bone specific training. It is thus noteworthy that the intervention causes highly significant BMB improvements anyway. Walking particularly increases BMD in the femoral neck, but impact loads rather affect the lumbar vertebrae. Combined loads will thus stimulate bone metabolism on more systemic levels [11,23,24]. This is in accordance with our findings and this supports the relevance of well-balanced, but possibly more specifically designed exercise patterns. However, details of figure 1 show that merely two subjects experienced transitions from catabolism to anabolism, *i. e.* shifts to $\delta^{44/42}Ca$ above -0.85 ‰. Here, individual changes, *i. e.* the random effects do matter.

Data analysis might appear needlessly elaborate. In fact, appropriate *t*-tests will validly reveal $^{44}Ca/^{42}Ca$ changes. This, however, precludes assessment of the covariates and of the detection of random effects correlations. The latter is particularly relevant. In sports science, it is commonplace that higher performance levels require disproportionately larger efforts to still achieve improvements. *Vice versa*, untrained subjects benefit exceptionally from small efforts. This eventually reflects fundamentals of biological adaptation.

Reduction of fracture risks during osteoporosis therapy is strongest for the most severely affected patients [25]. Fracture risk is not the primary end-point in the present study. But the finding fundamentally agrees with the negative correlation of the $\delta^{44/42}Ca$ intercepts and slopes. Strongly bone catabolic subjects thus experience disproportional benefits.

Age is generally considered the crucial factor for osteoporosis [25]. However, within the population investigated here, no corresponding effects were observed. This may be partly explained by comparably young ages and by correspondingly small scatter (57.0 ± 2.7 y). Moreover, intervals since the last menses were generally short (2-3 y). But, in fact, age itself is not proximate to the development of osteoporosis. Rather hormone concentrations take immediate effect. These, however, were merely employed as inclusion criteria. Most of the E2 values initially fell below the limit of quantitation (12 pg/ml). Possible changes of blood E2 thus went undetected.

Indeed, E2 drop is not exclusively responsible for postmenopausal bone loss [6]. Ennour-Idrissi *et al.* even observe decreases of E2 due to exercise [26]. This contradicts the putative responsibility of endocrine stimulation to the beneficial effects of exercise. Actually, intracrine estrogen production may be much more important [27]. Accordingly, lack of ovarian activity does not preclude effective intracellular E2 concentrations.

The BC-score well reflects the degree of obesity: The contributions of BM, BMI, FM, and AG to this measure are virtually identical. At the same time, SM, TBW, and LBM show close to identical contributions, but at opposite sign. The proportion of variance explained by the BC-score is extraordinary (92.5 %). Each single variable might hence serve as valid biomarker for obesity as well.

The relationship of BM and BMD is inconclusive [28]. In fact, positive relationships have been suggested. Due to increased mechanical stimulation, this appears feasible. But obesity may also result in negative BMB due to the stimulation of osteoclasts [29]. Sherk *et al.* [7] support this view. But Seifert *et al.* [6] did not observe correlations between BMI and bone loss during menopausal transition. Likewise, we did not observe significant effects of body composition on $^{44}Ca/^{42}Ca$. Moreover, none of the outstanding subjects (n=2, BMI > 30) showed conspicuous values.

The relevance of exercise to prevent osteoporosis is fundamentally undisputed [30]. But there is intense quest for optimal exercise patterns. While preferable for many other reasons, health-oriented walking alone does not appear very promising [30]. Walking is thought to impact rather specific skeletal sections. This is reflected by our finding that step equivalents do not exhibit impact on the rather systemic $^{44}Ca/^{42}Ca$ biomarker.

The F-score, *i. e.* the systematically combined strength performances (table 3) probably well approximates functional fitness. Its highly significant increase demonstrates the effectiveness of the training regimen. The initial F-scores and $^{44}Ca/^{42}Ca$ ratios are independent. So are the corresponding changes of both measures. This contradicts the findings of Sherk *et al.* [7] who observed BMD and strength data to be correlated. The authors employed localized BMD measurements and as stressed before, $^{44}Ca/^{42}Ca$ ratios advantageously rather reflect systemic BMB. The absence of any observable effects of the F-scores on $^{44}Ca/^{42}Ca$ is remarkable nonetheless.

We think that our findings suggest outstanding importance of regular exercise and of at least moderate, but balanced strength loads. This appears indispensable to bone health on the systemic level. Consistent with other studies [31] we conclude that few elaborate and individually adapted bouts per week are adequate. At least in respect to the intervals investigated here (12 w), exercise itself seems to outperform the effects of more specific covariates. Mere body weight training does seem to suffice. From the practioner’s perspective, this will represent a very beneficial result.

Conclusions

Moderate health focused training is suited to significantly improve general bone metabolism in postmenopausal women. Subjects with more catabolic metabolism experience disproportionate benefits. Significant and regular, if moderate, strength training loads are indispensable. $^{44}Ca/^{42}Ca$ analysis advantageously is capable to demonstrate corresponding adaptations on the systemic level.

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RESEARCH

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Resistance training alters body composition in middle-aged women depending on menopause - A 20-week control trial

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Abstract

Background Resistance training (RT) is effective in counteracting the age- and menopause-related loss of muscle mass (MM) and strength in middle-aged women (40–60 years). Research on RT with free weights is limited in pre- and post-menopausal women. Based on this, a 20-week training intervention was conducted with this population to investigate the effects of systematic RT with free weights on strength capacity and body composition.

Method Forty-one healthy women (52.0 ± 3.6 years) participated in this study. After 10-week control phase (no RT, T0-T1) followed by a 10-week intervention phase (T1-T2) with RT twice a week and 6–8 sets of each muscle per week. Subjects were randomly assigned to a low-intensity (50% 1-RM) or moderate-intensity (75% 1-RM) RT group and divided into pre-menopausal and post-menopausal according to their hormone profile. Fat-free mass (FFM), MM, fat mass (FM), muscle thickness (Vastus lateralis (VL), Rectus femoris (RF), Triceps brachii (TB)), grip strength, 1-RM squat and bench press were assessed before and after each phase. Statistical analysis was performed using a linear mixed model to account for fixed (time and group) and random (individual) effects.

Results A total of 31 women successfully completed the study. No injuries occurred during the intervention. Significant increases in 1-RM squat and bench press were observed in all groups. No interaction effect was observed for the strength parameters. In pre-menopausal women, FFM, MM and RF muscle thickness increased significantly, while VL showed a trend. These effects were not present in post-menopausal women regardless of RT intensity.

Conclusion RT with free weight is safe and effective for middle-aged women to increase 1-RM. Hypertrophy effects were found exclusively in pre-menopausal women. To achieve hypertrophy and/or body composition changes in post-menopausal women, larger training volumes (> 6–8 sets/muscle per week) are likely required.

Keywords Middle-aged women, Menopause, Hypertrophy, Muscle mass, Resistance training, Strength

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Introduction

Loss of muscle mass (MM) is part of the ageing process [1]. MM in men and women has been shown to decrease by 3 to 8% per decade after the age of 30, and by 5 to 10% after age of 50 [2]. This reduction in MM and also strength during the ageing process may lead to physical disability [1], negatively affects the performance of everyday life, and increases the risks of falls and fractures [1, 3]. For context, post-menopausal women with reduced MM show a 2.1-fold higher risk of falling and a 2.7-fold higher risk of bone fracture than women with preserved MM [4]. Furthermore, since skeletal muscle is a highly metabolically active tissue, common metabolic disorders associated with ageing, such as diabetes, may also be associated with the decline in MM [1]. Therefore, maintaining MM during the ageing process is crucial for musculoskeletal health [3, 5, 6].

Probably the most significant event for ageing women is menopause, which usually occurs approximately between the ages of 45 and 55 [7]. Menopause marks the end of menstruation and reproductive capacity and is associated with various physiological hormonal changes. In particular, the decline in estrogen levels has detrimental effects on body composition, such as an increase in fat mass (FM), a decrease in MM, strength, and bone mineral density (BMD) [1, 8–11]. Consequently, menopausal women are at higher risk of developing osteoporosis and other musculoskeletal disorders [11, 12]. Hormone replacement therapy is feasible but is associated with side effects such as breast tenderness, enlargement, headaches, mood changes, or nausea. As an alternative or in addition to hormone replacement therapy, exercise interventions may be recommended [13]. Resistance training (RT) has been shown to be particularly effective in counteracting most of the negative effects of the menopause described above. There is very good evidence that progressive RT in older adults has positive effects on lean body mass [1, 14, 15], MM [16–18], strength [3, 16, 17], functional capacity [19, 20], bone mass and BMD [3, 14]. Moreover, it reduces risks of falls and fractures [21] and promotes physical and mental well-being [22], confidence and happiness [23].

Therefore, it is not surprising that the World Health Organization recommends that all adults should do muscle-strengthening activities that involve all major muscle groups at moderate or greater intensity and at least twice a week to provide health benefits [24, 25]. Recent reviews show that strength and muscle growth can be achieved at any intensity and number of repetitions [26, 27]. It seems that only 5–6 sets per muscle group per week are sufficient for beginners to induce adaptations [26, 27]. But current recommendations are based on data from males. Only 2–14% of the articles in three major sports and exercise magazines included only women as participants [28].

Previous studies employing middle-aged and older women primarily made use of machine-based programs or a combination of machine and free weight exercises [29, 30]. In addition, research has tended to focus on the effects of low to moderate-intensity RT programs (around 60% 1-RM) and 8–12 repetitions [1, 30, 31] but this is not consistent with current recommendations. The National Strength and Conditioning Association's (NSCA) position statement on RT for older adults (i.e., >50 years of age) specifically recommends RT with 1–3 sets per exercise per muscle group, two to three days per week with free weight or machine-based exercises using multi-joint movements at an intensity of 70–85% 1-RM including repetition ranges from 8 to 15 [32]. Usually, 15 or more repetitions are completed at an intensity of 60%, or an intensity of 70–80% is generally used for a repetition range of 8–12 repetitions [26, 27]. Besides, only a few studies compared the effects of different intensities in machine-based RT programs [33, 34, 35, 36]. Moreover, "effort", or the set endpoint and exercise velocity was rarely described [29].

However, to increase strength, free weight training might be superior to machine-based programs [29, 32, 37]. In addition, movements of daily living can be ideally trained with free weights and are more akin to applied science [32]. It is therefore surprising that, to the best of our knowledge, no studies involving middle-aged or older women have been conducted exclusively with free weights. In summary, there is insufficient evidence to provide specific guidelines for older women, including pre-, peri-, and post-menopausal women, to optimize MM and strength gains [30]. Furthermore, participants' hormonal status was not or insufficiently assessed prior to enrollment [38], and there is a lack of data on the effects of free weight RT in middle-aged women.

Therefore, this is the first study to investigate the effects of free weight RT on muscle strength and body composition in middle-aged women depending on hormonal status (pre- and post-menopausal) and two different intensities. This will include identifying potential differences in the development of fat-free mass (FFM), MM, and strength capacity, as well as FM reduction, according to pre- and post-menopausal status.

Methods

Participants

To determine the sample size, a power analysis (F-tests, Anova: Fixed effects, special, main effects and interaction) was performed a priori. For the calculation, a medium to strong effect (f) (0.25–0.40), an α-error of 0.05, and a power of 0.8 (1-β error) were specified. Based on the three-arm model (df=2), a total sample size of 18–36 subjects was calculated. However, since the study will last for a total of 20 weeks and drop-outs were taken into account, the number of subjects was set at a minimum of 40. All volunteers had to be healthy, with no orthopedic or cardiovascular complaints and should be able to perform a squat with the tops of their thighs parallel to the floor. As a result, seven individuals were excluded before the start of the study. After being informed about the study procedures and inclusion criteria, 41 healthy women were enrolled in the study (15/03/2021) after signing informed consent. The classification of the participants as pre-menopausal and post-menopausal was based on hormone concentrations and the date of the last menstrual period [38]. Participants were classified as post-menopausal if they had low estradiol (E2) and high follicle-stimulating hormone (FSH) and had not menstruated for at least 12 months [38]. Seventeen participants (n = 17) were classified as pre- (PreMeno) and 24 as post-menopausal (PostMeno). Subsequently, PostMeno women were allocated to two subgroups after stratified randomization (MM, age, weight and height): moderate-intensity (MI-RT; n = 12) and low-intensity (LI-RT; n = 12). PreMeno women were not subdivided due to the small sample size and performed MI-RT.

Experimental design

The study was approved by the local ethics committee of the IST University of Applied Science, Dusseldorf (02/2021), according to the Declaration of Helsinki, and registered in the German Registry of Clinical Studies (05/03/2021; DRKS00023826). In addition, the hygiene concept to prevent the spread of COVID-19 was approved by the local regulatory authority. A total of 41 women aged 40–60 years were recruited into a local gym. The study design encompassed two phases, and three measurement points (T0, T1, T2), and lasted for 20 weeks (see Fig. 1).

Initially, ten weeks (T0-T1) served as a control period without any training or systematic physical activity to examine the effects of reduced physical activity (gym lockdown due to the COVID-19 pandemic) on strength capacity and body composition. This was followed by a 10-week RT intervention period (T1-T2) using a two-group matched pair parallel design. At T0, participants completed questionnaires about their health, menstrual status, and recent RT history. Subsequently, hormone status (E2, progesterone (P), (FSH), testosterone (T), dehydroepiandrosterone (DHEA)), body composition (total body water (TBW), FFM, MM, FM), muscle thickness (vastus lateralis (VL), rectus femoris (RF), triceps brachii (TB)), grip strength (GS), and dynamic strength (1-RM squat (SQ), 1-RM bench press (BP)) were assessed. The same variables were also collected after the control and RT period except for hormone status. T2 testing was done 48–72 h after the last RT session.

Procedures

Forty-eight hours before testing, the subjects were not allowed to engage in RT or any other strenuous physical activity. The volunteers were also not allowed to drink alcohol or coffee before testing and had to appear in a fasted state. However, about 300-400ml of water had to be drunk in the morning to equalize the water balance. All measurements (T0–T2) were conducted single-blind in the morning (7.30–11.00 am) at the same time of the day by the same researcher.

Hormone parameters

The saliva and blood samples were collected immediately at the beginning of T0 (7.30-9.00am). In premenopausal women, saliva and blood samples were collected during the luteal phase (second half of the cycle), when both E2 and P concentrations are high. Hormone concentrations were used only for identification and classification between pre- and post-menopausal states. For saliva samples, specific ELISA kits for E2, P, T, and DHEA

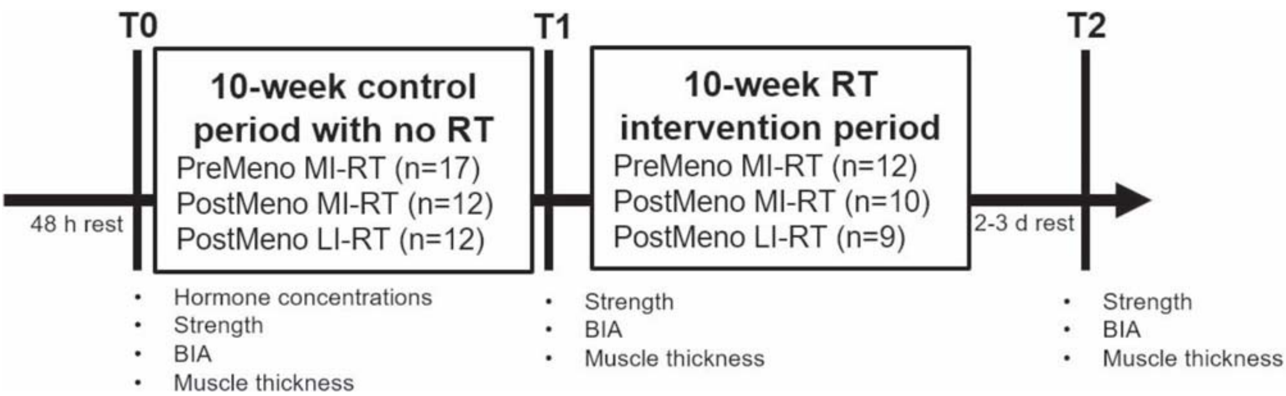

Fig. 1 Schematic representation of study design. RT = resistance training; BIA = bioelectrical impedance analysis; PreMeno = pre-menopause; PostMeno = post-menopausal; MI-RT = moderate-intensity resistance training; LI-RT = low-intensity-resistance training

concentrations were used (RE52281; RE62141; RE52651; RE30121046; Re62039). Dry blood concentration of FSH was analyzed by an external laboratory according to the CLIA method (Ayumetrix, 17,387 63rd Ave, Lake Oswego, OR 97,035, USA).

Body mass and body composition

Body weight (BW) and body composition were measured immediately after collecting salvia and blood samples. BW was assessed using a digital scale (Etekcity EB4074C, Anaheim, CA, United States of America), with participants wearing only underwear and no shoes or socks. TBW, FFM, MM, and FM were analyzed by bioelectrical impedance analysis (BIA 101, Akern, Firenze, Italy). BIA 101 Akern is a valid and reliable alternative method to dual-energy X-ray absorptiometry (DXA) for verification of body composition [39, 40]. BIA was performed using an alternating sinusoidal electric current of 400 microampere at an operating frequency of 50 kHz. For the bioelectrical impedance measurement, each participant was supine with limbs slightly spread apart from the body for 10 min to allow for fluid shift [41]. Disposable tab electrodes (BIATRODES Akern Srl; Florence, Italy) were placed on the right side at metacarpal and metatarsal sites of the right wrist and ankle [39]. Subsequently, the measurement was performed, and the data were processed using BodyGramPro software (Version 3.0, Akern, Firenze, Italy). Further information about the BIA 101 can be obtained from the manufacturer's manual [42].

Muscle thickness

For muscle thickness measurements, a B-mode ultrasound (Mindray DP-50, Mindray Medical International Ltd, Shenzhen, China) with an 8.5-MHz linear probe (Mindray 75L53EA, Mindray Medical International Ltd, Shenzhen, China) was used. Muscle thickness was measured at three sites in the muscles on the right side, in accordance with previous studies [41, 43].

M. vastus lateralis thickness was measured with the participants lying on their left side on an examination table at half the distance between the most prominent point of the greater trochanter and the lateral condyle of the tibia (gain 50 dB; image depth 3.7 cm). The thickness of the rectus femoris was measured at 50% between the anterior inferior supra iliac crest and the proximal border of the patella with participants lying supine (gain 50 dB; image depth 3.7 cm).

For measurement of the triceps brachii, the participants lay in the prone position while images were taken at 40% distal between the acromial process of the scapula and the lateral epicondyle of the humerus (gain 50 dB; image depth 5.5 cm). To ensure the identical positioning of the ultrasound probe, the measuring points were marked with a waterproof pen. Ultrasound transmission gel was applied to the probe head and the probe was positioned perpendicular to the long axis of the extremity without depression of the underlying tissue. Three images were recorded at each site and stored on a USB flash drive. Subsequently, muscle thickness was analyzed in the images using the caliper measurement of the ultrasound device. The mean values of the three images of each site were used for further analyses. The test–retest intraclass correlations coefficient for this analysis was reported from our laboratory as 0.998 (RF), 0.996 (VL), and 0.997 (TB) [41].

Maximum strength tests

Following a standardized warm-up procedure (5 min running), grip, upper and lower body strength tests were conducted. Grip strength of both hands was assessed using a digital hand-held dynamometer (digital Jamar+, Fabrication Enterprises, New York, United States). For testing, volunteers were seated upright on a chair with their elbows bent at 90° and in contact with the body. Then they were instructed to press the handle of the device as forcefully as possible for at least five seconds without changing their position. Three trials were carried out for each side. Maximum strength was measured alternately. The rest period between repetitions on each side was 120 s. The best trial was documented for further analysis. For testing lower body strength, a "touch and go" barbell box squat (femur parallel to the floor, 90° knee angle) was used. The height of the box was individually adjusted for each subject and maintained throughout the RT period and during retesting. After a minimum of five minutes of rest, upper body strength was assessed using the free weight BP exercise. For this, grip widths were documented and stipulated throughout the study. For both tests, the participants first completed ten repetitions with an empty bar, followed by a two-minute rest period. A second warm-up set of ten repetitions was then performed with at approximately 50% of the predicted ten-repetition maximum load. Following four-minute rest, a final set was performed to the point of momentary concentric muscle failure or failure of proper exercise technique. This was done by pre-setting a load that the research team estimated would allow one to ten repetitions. Both exercises are well-established exercises for determining strength ability and upper and lower body performance [44]. From the load used and the number of repetitions completed, the 1-RM SQ and BP were calculated according to the formula proposed by Brzycki [45], which was considered sufficiently accurate for estimating 1-RM using fatiguing sets of less than ten repetitions [46].

Resistance Training Protocol

A detailed description of the RT protocol (sets, repetitions, intensity, tempo, and rest) throughout the study can be found in Table 1. The training program consisted of two cycles of five weeks each. Weeks one to four of each cycle were "loading" weeks, followed by one "deload" week. Deload weeks were introduced to counteract possible over reaching due to too rapid increases training weights. Training was performed twice weekly, 48–72 h apart. All RT sessions were supervised by a qualified member of the research team (researcher-to-participant ratio 1:1–4). Exercise selection was identical for all intervention groups. Session 1 consisted of "touch and go" barbell box squats (femur parallel to the floor), barbell bench press, seated neutral grip cable row, dumbbell side bend, and prone plank. In the second training session, the same exercises were repeated, except that the cable row was replaced by a lat pull-down with a wide pronated grip. Except for the box squats and the plank, all exercises were performed with the maximum range of motion possible and at identical tempo. Volume loads (repetitions x sets x % 1-RM) were approximately similar between the intervention groups, with the MI-RT group performing more sets per exercise to achieve a similar volume load compared to the LI-RT group. The adjusted weight of the box squat and bench press in the first cycle was based on the initial 1-RM test (T1), whereas the resistance of the remaining exercises was determined by trial and error. During the "loading" weeks, the last set of each exercise was performed to momentary concentric failure or failure of proper exercise technique. In the following weeks, the weight for each exercise was increased by 2.5-5%, depending on the number of repetitions to failure. From the last set of each exercise in week 4, a new 1-RM was estimated using the Brzycki formula [45] and used from week six.

Table 1 Overview of the resistance training protocol

	Cycle 1		Cycle 2	
	Week1–4 Loading	Week5 Deload	Week6–9 Loading	Week10 Deload
	Session 1 and 2 (sets x reps)			
MI-RT	**4sets**	**3sets**	**4sets**	**3sets**
Intensity (% 1-RM)	3×10 1x to failure 75 [1)]	3×10 53.3[1)]	3×10 1x to failure 75[2)]	3×10 53.3 [2)]
LI-RT	**3sets**	**2sets**	**3sets**	**2sets**
Intensity (% 1-RM)	2×20 1x to failure 50[1)]	2×20 40[1)]	2×20 1x to failure 50[2)]	2×20 40[2)]
Tempo (s)	2:0:1 (eccentric : isometric : concentric)			
Rest (s)	120 s			

MI-RT = moderate-intensity resistance training group; LI-RT = low-intensity resistance training; 1-RM = one-repetition maximum;[1)]based on pre intervention 1-RM; [2)]based on estimated 1-RM using the Brzycki formula (35) (weight and repetitions from the last set of each exercise following week 4 session 2)

Nutrition

Dietary habits were maintained throughout the 20 weeks. Participants were unfamiliar with comprehensive nutrition documentation and related tools, so it was not possible to establish it as standard practice from the outset. Further, due to the COVID-19 pandemic, it was not possible to provide more comprehensive and specific nutritional recommendations. Only immediately after the RT sessions was the diet standardized. Participants consumed a carbohydrate-protein source and could choose between three different carbohydrate and protein rich meals. Each meal has been used in previous investigations [47, 48]. Detailed meal information is provided in the supplementary material.

Statistical analyses

Data were analyzed by the R statistical language version 4.0.4 (R Core Team, 2021). Only data from participants with an adherence of >85% were included in the analyses. The raw data of VL, RF, and TB were box-cox transformed prior to analysis. The transformation was applied to obtain approximately Gaussian distributions of the raw data, which otherwise exhibited highly skewed distributions. Transformations were applied to the data at T_0 and the box-cox estimates for λ were then employed to transform the remaining data.

The values of FFM, MM, FM, GS, 1-RM SQ and BP were analyzed unchanged. Individual time intervals (Δt [h]) since the start of the study were introduced as an additional covariate. Data analysis was performed using linear mixed effects (LME) models with $FFM_λ$, $MM_λ$, $FM_λ$, $VL_λ$, $RF_λ$, $TB_λ$, GS, 1RM SQ and BP used as dependent variables. Model building was performed independently for each of these.

We were specifically interested in the effects of menopause on the trends of strength capacity and muscle growth. Therefore, all models included the interaction term of menopause with PreMeno MI-RT (T0 to T2) as a fixed effect. Likewise, PreMeno MI-RT itself was axiomatically included as a fixed effect. As it represents an ordered factor with three levels, second-order orthogonal polynomials were chosen as contrasts for PreMeno MI-RT.

Initially, random effects were merely assumed between the individual intercepts of each measure. Subsequently, Δt was included as a random effect, where linear individual trends were assumed. The presence of potentially non-linear individual trends was then investigated by upgrading to 2nd or 3rd-order natural splines of Δt. After developing appropriate random effect structures, it was tested whether Δt also contributed to general trends in the population, i.e., whether it represented a significant fixed effect. In either case, model comparisons were based on likelihood statistics and changes in Akaike's information criterion. Significant differences were set at $p \leq .05$.

Finally, effect sizes between discrete time levels were determined according to the approximation of Cohen's *d* for mixed effects models ($d = 2t/DF^{(1/2)}$) where t = t-value; DF = degrees of freedom. Classifications were stipulated as follows: trivial < 0.2; small < 0.5; moderate < 0.8; strong > 0.8 [49]. All graphs were created using the latest version of GraphPad Prism.

Results

Five participants missed T1 testing and were therefore excluded from the second part of the study. Another five participants missed more than three RT sessions during the intervention period (T1–T2) and were therefore also excluded from the final analysis. The reasons for absence were non-study-related injury or illness (n = 4) and other personal reasons (n = 6). No injuries occurred during the RT intervention. In total, 31 subjects completed the study. The PreMeno women (n = 12) had an average age of 47.4 ± 5.3 years and a height of 167.5 ± 8.4 cm. The PostMeno MI-RT group (n = 10) had an average age of 54.3 ± 4.7 years and a height of 166.0 ± 7.2 cm. The anthropometric data for the PostMeno LI-RT group (n = 9) were 55.6 ± 2.9 years and 166.6 ± 5.9 cm. The hormone concentrations of the three training groups at T0 are shown in Table 2.

Body composition

BW and body mass index (BMI) did not change significantly in none of the three groups during the entire period (BW: $p = .494$; BMI: $p = .559$). No difference between the groups could be determined for the BW (PostMeno MI-RT: $p = .992$; PostMeno LI-RT: $p = .131$) and BMI (PostMeno MI-RT: $p = .503$; PostMeno LI-RT: $p = .115$).

For FFM, only a significant increase was observed in the PreMeno MI-RT group ($p = .015$) (first order). The effect between T1 and T2 in the PreMeno MI-RT group was small ($d = 0.29$). In addition, an interaction effect (first order) of both PostMeno and PreMeno MI-RT could be identified (PostMeno MI-RT: $p = .032$; PostMeno LI-RT: $p = .022$). Unlike the PreMeno MI-RT group, the two PostMeno groups showed no increase in FFM (Fig. 2a).

In MM, only a significant increase was observed in the PreMeno MI-RT group ($p = .002$) (second order). The effect between T1 and T2 in the PreMeno MI-RT group was strong ($d = 1.25$). Additionally, the group effect (second order) of both PostMeno and PreMeno MI-RT could be identified (PostMeno LI-RT: $p = .030$; PostMeno LI-RT: $p = .024$). Unlike the PreMeno MI-RT group, the two PostMeno groups did not have an increase in MM (Fig. 2b).

In FM, only a significant decrease was detected in the PreMeno MI-RT group ($p = .039$) (first order). The effect between T1 and T2 in the PreMeno MI-RT group was moderate ($d = 0.57$). A Time*group interaction was only between the PostMeno LI-RT to the PreMeno MI-RT group ($p = .039$) (second order). In contrast to the PreMeno MI-RT group both PostMeno groups had no decrease in FM (Fig. 2C).

Table 2 Hormone concentration

	PreMeno MI-RT	PostMeno MI-RT	PostMeno LI-RT
E2 (pg/ml)	7.4 ± 17.1	1.1 ± 1.0	1.5 ± 1.2
P (pg/ml)	58.4 ± 40.2	51.2 ± 24.5	30.3 ± 11.8
FSH (mIU/ml)	16.7 ± 19.0	86.2 ± 33.9	96.5 ± 16.7
T (pg/ml)	14.4 ± 6.4	15.7 ± 7.9	16.0 ± 8.2
DHEA (pg/ml)	170.9 ± 72.0	195.6 ± 90.6	179.9 ± 77.9

PreMeno = pre-menopause; PostMeno = post-menopause; MI-RT = moderate-intensity resistance training; LI-RT = low-intensity resistance training;DHEA = dehydroepiandrosterone; E2 = estradiol; FSH = follicle-stimulating hormone; n.a. = no analyses; P = progesterone; T = testosterone

Muscle thickness

A significant difference over time was observed in the RF ($p = .004$) (first order). Different curve progression could not be detected (PostMeno MI-RT: $p = .210$; PostMeno LI-RT: $p = .300$) (first order). The effect between T1 and T2 in all groups was moderate to strong (PreMeno MI-RT: $d = 0.80$; PostMeno MI-RT: $d = 0.46$; PostMeno LI-RT: $d = 0.52$) (Fig. 3a).

Trends over time could be identified in the VL (first order: $p = .050$; second order: $p = .079$). In the PreMeno MI-RT and PostMeno MI-RT groups, a small to moderate effect was found between T1 and T2 (PreMeno MI-RT: $d = 0.54$; PostMeno MI-RT: $d = 0.43$). In addition, a trend in the curvature could be observed between the PreMeno MI-RT and the PostMeno LI-RT group ($p = .058$) (first order) (Fig. 3b).

In the TB, no significant difference over time could be detected (first order: $p = .72$; second order: $p = .83$). In addition, no group differences were observed (Fig. 3c).

Strength

All three groups increased their SQ performance significantly over time (first order: $p = .000$ and second order: $p = .002$). No group differences were observed in SQ performance (PostMeno MI-RT: $p = .257$; PostMeno LI-RT: $p = .913$ first order) (Fig. 4A). A strong effect was detected over time for all groups (PreMeno MI-RT: $d = 1.51$; PostMeno MI-RT: $d = 1.52$; PostMeno LI-RT: $d = 1.64$ s order). Each group improved significantly in BP performance (first order: $p = .000$ and second order: $p = .000$) (Fig. 4B).

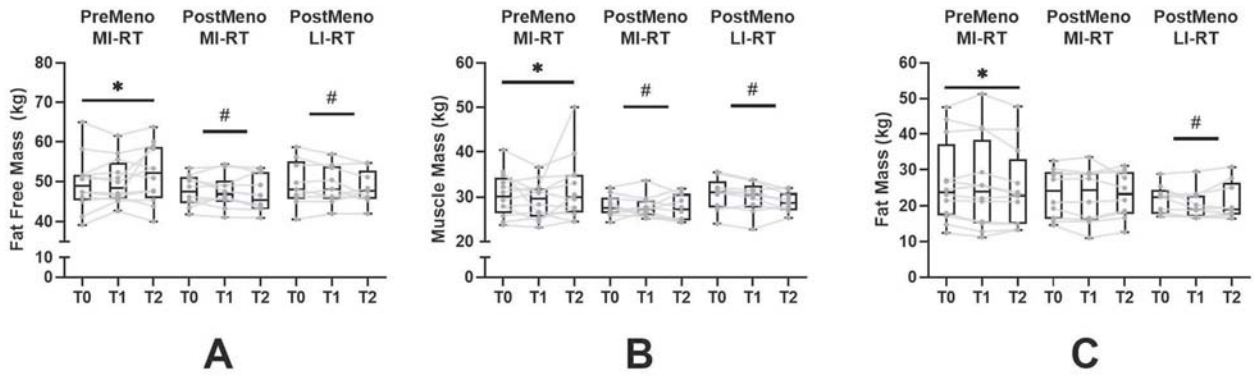

Fig. 2 Body composition: fat-free mass, muscle mass, fat mass. Significant time and time*group effects were set p < .05. Time effects were marked with * and group effects with #

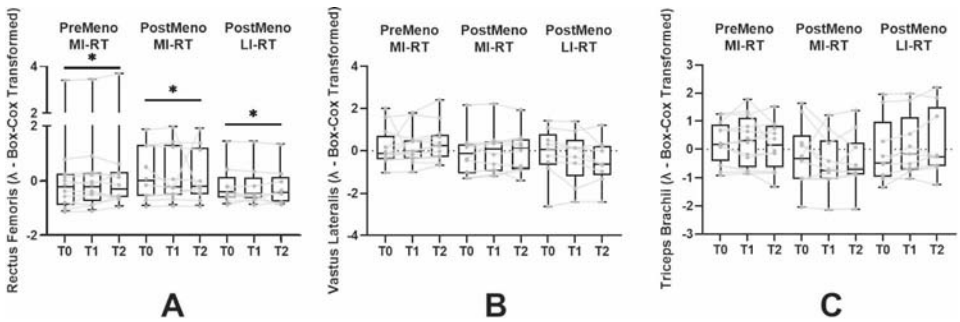

Fig. 3 Muscle thickness of m. rectus femoris, m. vastus lateralis, m. triceps brachii. Significant time and time*group effects were set p < .05. Time effects were marked with * and time*group effects with #

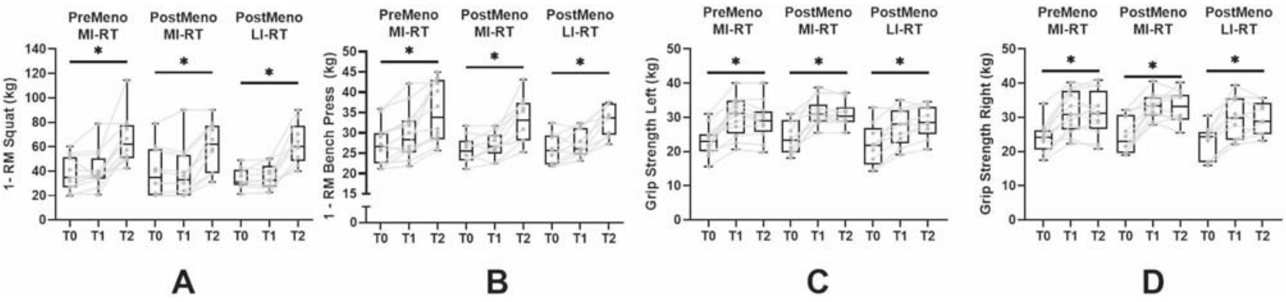

Fig. 4 Strength parameter: 1-RM squat, 1-RM bench press, grip strength. Significant time and time*group effects were set at p < .05. Time effects were marked with * and time*group effects with #

No significant difference in curve progressions could be observed between the groups. (PostMeno MI-RT: $p=.712$; PostMeno LI-RT: $p=795$, first order). A moderate to strong effect over time was detected for each group (PreMeno MI-RT: $d=0.66$; PostMeno MI-RT: $d=0.98$; PostMeno LI-RT: $d=0.84$ second order). In grip strength, an identical development was found for the left and right hand and was summarized as one score. Both the first and second-order terms were significant (first order: $p=.000$ second order: $p=.000$) (Fig. 4C&D). No differences were detected between the three groups (PostMeno MI-RT: $p=.548$; PostMeno LI-RT: $p=.675$, first order).

All results are summarized in Table 3.

Discussion

This study investigated, the effectiveness of systematic RT using free weight on strength, and body composition in middle-aged women (40–60 years). For this purpose, a 20-week intervention with a 10-week control-phase and a 10-week training phase was conducted. The results show different effects on body composition for PreMeno and PostMeno women, but not on strength gains. PreMeno

Table 3 all results of body composition, muscle thickness and strength capacity

	PreMeno MI-RT			PostMeno MI-RT			PostMeno LI-RT		
	T0	T1	T2	T0	T1	T2	T0	T1	T2
Age (y)	47.4 ± 5.3			54.3 ± 4.7			55.6 ± 2.9		
Height (cm)	167.50 ± 7.99			166.00 ± 6.78			166.56 ± 5.58		
BW (kg)	76.19 ± 16 0.31	76.18 ± 16.18	75.62 ± 16.54	70.29 ± 8.61	70.43 ± 8.83	70.04 ± 8.33	71.10 ± 8.52	69.68 ± 7.90	69.56 ± 8.35
BMI (kg/m^2)	27.28 ± 5.78	27.25 ± 5.95	27.03 ± 5.82	25.81 ± 2.15	25.52 ± 2.48	25.37 ± 2.26	25.62 ± 2.79	25.06 ± 2.90	25.12 ± 3.06
FFM (kg)	**49.58 ± 6.78**	**50.08 ± 5.41**	**51.97 ± 6.99***	**47.70 ± 3.63**	**48.07 ± 3.89**	**46.99 ± 4.41#**	**49.49 ± 5.47**	**49.20 ± 4.61**	**48.46 ± 4.00#**
MM (kg)	**30.48 ± 4.77**	**29.18 ± 3.95**	**31.88 ± 7.05***	**27.98 ± 2.22**	**27.78 ± 2.34**	**27.59 ± 2.74#**	**30.56 ± 3.47**	**29.80 ± 3.24**	**28.77 ± 2.09#**
FM (kg)	**26.44 ± 11.13**	**26.09 ± 12.22**	**24.82 ± 10.77***	23.49 ± 6.40	22.84 ± 7.25	23.10 ± 6.07	**21.61 ± 3.74**	**20.48 ± 3.93**	**21.32 ± 4.85#**
VL (cm)	**2.39 ± 0.42**	**2.40 ± 0.45**	**2.62 ± 0.48***	**2.25 ± 0.48**	**2.29 ± 0.53**	**2.41 ± 0.51***	**2.26 ± 0.56**	**2.15 ± 0.62**	**2.15 ± 0.55§**
RF (cm)	**1.95 ± 0.85**	**1.98 ± 0.84**	**2.18 ± 0.85***	**2.13 ± 0.66**	**2.07 ± 0.68**	**2.23 ± 0.66***	**1.84 ± 0.48**	**1.77 ± 0.49**	**1.95 ± 0.47***
TB (cm)	3.29 ± 0.39	3.29 ± 0.47	3.26 ± 0.46	3.01 ± 0.58	2.87 ± 0.50	2.96 ± 0.54	3.11 ± 0.60	3.20 ± 0.56	3.31 ± 0.66
GS left (kg)	**23.12 ± 4.16**	**30.32 ± 5.51***	29.16 ± 5.26	**24.16 ± 4.53**	**31.52 ± 3.78***	30.96 ± 3.46	**21.99 ± 5.84**	**27.20 ± 5.11***	28.74 ± 4.39
GS right (kg)	**23.95 ± 4.28**	**31.45 ± 5.72***	31.27 ± 6.23	**24.59 ± 5.01**	**33.30 ± 3.61***	33.09 ± 4.48	**22.68 ± 4.76**	**29.80 ± 5.85***	29.76 ± 4.46
1-RM SQ (kg	**37.91 ± 12.99**	**40.85 ± 14.83**	**65.80 ± 18.76***	**39.01 ± 19.64**	**36.83 ± 21.45**	**60.71 ± 18.91***	**34.27 ± 8.07**	**35.49 ± 9.20**	**62.77 ± 15.87***
1-RM BP (kg)	**27.24 ± 4.86**	**29.77 ± 5.92**	**35.12 ± 7.10***	**25.83 ± 3.19**	**27.01 ± 2.95**	**33.05 ± 5.45***	**25.98 ± 3.58**	**27.47 ± 3.18**	**33.38 ± 3.62***

PreMeno = pre-menopause; PostMeno = post-menopause; MI-RT = moderate-intensity resistance training; LI-RT = low-intensity resistance training; FFM = fat-free mass; FM = fat mass; MM = muscle mass; VL = vastus lateralis; RF = rectus femoris; TB = triceps brachii; GS = grip strength; 1-RM SQ = one repetition maximum squat; 1-RM BP = one repetition maximum bench press; Significant time effects were set at $p \leq .05$ and *were marked with *. If no difference was identified between the groups over time, this was assumed for all groups. Time*group differences were marked with #. The Premeno MI-RT group was used as a control treatment and the curves of the two post-menopausal groups were compared. Trends (*$p < .10$*) showing potential statistical differences between two groups and were marked with §*

women with higher E2 concentrations and an active menstrual cycle significantly increased their FFM (small effect), MM (strong effect) and muscle thickness in VL (moderate effect) compared to PostMeno women regardless of training intensity. However, similar increases in lower and upper body strength as well as grip strength were achieved in all groups. In contrast to the hypertrophy effects, there appear to be no differences depending on hormone concentrations.

In general, there is a lack of studies on RT in middle-aged women using free weights only. However, flexion and extension movements in the hip joint, as well as traction and compression stresses on the shoulder joint, are everyday strains for active individuals. Free weight exercises such as squats and bench presses, which can simulate movements of daily living, may be ideal for increasing strength at a high level of specificity [29, 37, 50]. There are currently no studies comparing the effects of free-weight RT alone with machine-based interventions in PreMeno or PostMeno women. However, the present study has shown that free weight RT can be used safely and effectively in middle-aged women. In addition, our results demonstrate that low and moderate-intensity RT using free weights is effective for increasing strength in PreMeno and PostMeno women, both in the upper and lower body. These findings corroborated observations from previous studies based on younger participants [37, 51, 52]. For example, Botero and colleagues showed that three RT sessions per week over 12 months could increase BP and leg press performance [53]. The strength increases in our study are comparable to the effects reported in previous research [54, 55]. In comparison, Karaslaan and colleagues showed a stronger effect with 4 training sessions/week for 12 weeks with machine-assisted training [56]. Similar to the male participants, the studies on middle-aged women show a comparable dose-response relationship in the adaptation processes of muscular strength [57]. Interestingly, this study did not find any differences between PreMeno and PostMeno women. The change in endocrine homeostasis probably has no significant effect on strength capacity in untrained healthy middle-aged women. In this population, other factors such as neuronal activation presumably could play an important role in the first few weeks of RT. At present, however, there is no indication of how many training experiences are needed to rule out strong neural adaptations and rather attribute the effects to endocrine homeostasis for strength adaptations. Therefore, the influence of endocrine homeostasis in trained women cannot be answered at this time, as no studies are available.

Compared to dynamic strength, there was no increase in isometric grip strength in any group after the training intervention. On the contrary, a significant increase was observed in all groups at the end of the first phase, despite this phase being a control period without RT. The adaptation effects were more likely due to learning effects, as no RT was performed at this time. Surprisingly, grip strength did not improve during the subsequent intervention period, although most of the exercises undertaken require a strong grip, e.g. lateral flexion, barbell row and lat pull, which could have yielded improvements in grip strength. Similar to the data presented here, RT on machines for 12 weeks and three training sessions per week had no effect on grip strength [58]. Interestingly, grip strength is an important predictor of muscle status [59] and it is regularly employed to estimate the risk of all-cause mortality in the elderly [60]. However, if total body strength, but not grip strength, can be improved by RT with free weights, the relationship between grip strength, muscle status and therefore mortality may need re-examination.

Unlike muscular strength, significant differences between PreMeno and PostMeno women could be identified for FFM and MM. Significant curve progression was only observed in the PreMeno MI-RT group. A negative trend was also observed in the PostMeno LI-RT group. Compared to the PostMeno MI-RT group, MM decreased by -1.8±2.0 kg between T0 and T2 (Table 3). Although there is no significant difference between PostMeno MI-RT and PostMeno LI-RT, the first indices suggest that this trend could not be observed in the PostMeno MI-RT group (-0.4±2.4 kg). These results are in line with the observations of Karaaslan et al., who observed a significant decrease in lean body mass despite a 12-week intervention with 4 low intensity (40–50% 1-RM) training sessions per week. This result was not observed in the higher-intensity training group (70–80%) [56].

Training volume may also influence muscle growth in PostMeno women. Several attempts have been made to compare low-volume and high-volume training in RT research with elderly women [52, 55, 61–66]. For example, the results of Oliveira et al. showed that a higher training volume per week induced greater muscle growth in PostMeno women than low-volume training [61]. Both intervention groups performed machine-based training at an intensity of 80% 1-RM over 12 weeks with 3 training sessions each. The high-volume group had a total of 15 sets per exercise per week from week 3, whereas the low-volume group had only nine sets per week per exercise [61]. Radaelli et al. reported significantly greater quadriceps growth after 20 weeks of high-volume resistance training (6 sets per exercise per week) compared to low-volume resistance training (2 sets per exercise per week) [63]. Interestingly, similar to other studies [62, 64, 65], the authors reported training volume in terms of sets per exercise per week. However, very often the actual training volume per muscle group is higher than reported because training protocols include, for example, leg press exercises as well as leg extension or leg curl exercises. In Radaelli et al. [63], for instance, the high-volume group actually performed 12 sets of direct quadriceps training whereas the low-volume group performed 4 sets of direct quadriceps training, giving a more accurate picture of training volume distribution. Consequently, in both studies [61, 63], the high-volume groups performed more training sets per week per muscle group than the PostMeno LI-RT (six sets per week) and the PostMeno MI-RT (eight sets per week).

Importantly, not all studies found significant differences in favor of high-volume interventions compared to low-volume interventions for muscle growth [62, 64, 65]. However, in another study by Radaelli et al., the authors reported larger effect sizes after 6 weeks of training in high-volume protocols (12 sets of quadriceps training per week) compared to low-volume protocols (4 sets of quadriceps training per week) in the VL (effect size (ES)=0. 33 vs. ES=0.21), RF (ES=0.28 vs. ES=0.13), vastus medialis (ES=0.37 vs. ES=0.11), vastus intermedius (ES=0.20 vs. ES=0.14) and total quadriceps (ES=0.45 vs. ES=0.21) [64]. Similarly, Cunha and colleagues reported comparable significant increases in lean soft tissue between high-volume training (9 sets per exercise per week) and lower-volume training (3 sets per exercise per week), although slightly higher percentage changes (calculated by the authors of the present study) are observed in favor of high-volume training (appendicular lean soft tissue: 6.2% vs. 6.9%; upper limb lean soft tissue: 7.8% vs., 8.8%; lower limb lean soft tissue: 5.6% vs., 6.3%) [65]. Both groups performed exercises such as chess press, leg press, knee extension and leg curl. In common with previous studies, training volume was not reported for each muscle group, leading to the assumption that more volume was executed per muscle group than reported. Therefore, it can be speculated that PostMeno women require higher training volumes to induce greater muscle hypertrophic adaptations. Future studies should aim at longer intervention studies comparing higher training volumes with free weights (>10 sets per muscle group per week) and lower training volumes (<10 sets per muscle group per week).

Kang and colleagues also observed significant muscle growth with RT after 12 weeks [58]. Similar to de Oliveira, three training sessions with three sets per exercise were performed. In contrast to de Oliveria and the conducted intervention, a total of seven exercises were performed. The intensity of the exercises ranged from 55 to 65% 1-RM [58]. Consequently, it can be assumed that hypertrophy can be also induced with a higher training volume with moderate-intensity. In contrast to the BIA results as an indirect method of measuring MM, muscle thickness measurements showed a significant increase in RF over time, but no group differences. Moreover, in VL a trend over time ($p=.050$) and different curve progressions ($p=.058$) could be detected between the PreMeno MI-RT and PostMeno LI-RT groups. These results suggest that MI-RT results in superior adaptations in terms of muscle thickness compared to LI-RT. This is in line with the BIA results. However, there are no comparable data from previous studies.

FM decreased significantly only in the PreMeno MI-RT group. The results of both PostMeno groups do not confirm the observations of previous studies. Both Kang et al. [58] and Delshad et al. [67] observed a significant decrease in body fat after 12 weeks of RT. Similar to the effects on MM, training frequency and volume also play a decisive role in FM. This assumption can be supported by the results of Rodrigues et al., who found that FM did not decrease in a 12-week intervention study with two training sessions per week, including RT and endurance exercises [68]. The intensity of the training was controlled by a subjective Effort Perception Scale, which kept the intensity between 13 and 15 [68]. Therefore, both the intensities and frequencies of the resistance training and endurance parts were presumably too weak to activate fat metabolism.

Limitations

Besides the important new findings, this study also has some limitations. One important factor is the small sample size of the individual training groups, so the observations must be regarded as preliminary evidence. Although there was a high level of interest in this study among women in this age group, almost 15% of those interested had to be excluded before the study started because of lack of mobility. In addition, training sessions were quickly cancelled for family reasons. Nevertheless, all participants reported that they enjoyed free weight training and were able to manage their daily lives better.

Another limitation of this study is the documentation of diet during the intervention. It was not possible to monitor the diet of all participants with a food diary over the entire duration. Therefore, only the protein and carbohydrate intakes immediately after exercise were ensured in order to stimulate protein biosynthesis as quickly as possible and to promote recovery in the best possible way. Even though the participants were instructed not to change their diet, this could also affect the results. Furthermore, it is not possible to say whether the participants had a sufficient protein intake to promote muscular adaptation in the best possible way. Therefore, future studies in this population should consider the effects of diet, and especially protein intake. Due to the hormonal changes and body composition in post-menopausal women, protein intake should be calculated based on FFM to ensure the best possible feasibility.

We additionally collected saliva and blood samples from premenopausal women once at T0. Although E2 and P are highest during the luteal phase when we collected our samples, its rather speculative whether the highest concentrations of E2 and P were obtained given that E2 and P vary during the menstrual cycle and the luteal phase itself. [69].

Conclusion

In conclusion, the results of this study show that free weight RT is generally safe and effective for middle-aged women. Free weight, moderate-intensity RT twice a week leads to an increase in 1-RM squat and bench press performance, as well as an increase in muscle mass and a decrease in fat mass in pre-menopausal middle-aged women. In post-menopausal women, RT induces an increase in dynamic strength but not in muscle mass, which can be induced by RT irrespective of intensity. However, there is some evidence that a higher intensity led to better effects on muscle mass. It seems that the general recommendations for anaerobic exercises, such as resistance training, do not lead to increases in muscle mass and decreases in fat mass in post-menopausal women [24, 70]. It appears that post-menopausal women require more than two training sessions and more than six to eight sets per muscle group/week, as well an intensities of more than 50% 1-RM elicit changes in body composition. These hypotheses are supported by two meta-analyses of dose-response relationships in elderly [71, 72].

Supplementary Information

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Supplementary Material 1

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Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by DK, TH, AE, and UF. The first draft of the manuscript was written by EI, KH, and SG and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data Availability

The raw data of the participants can be requested from the corresponding authors if required. All data was encrypted so that it cannot be traced back to individual persons.

Declarations

Competing interests

The authors declare no competing interests.

Consent publication

All authors and participants agree to publish the collected data anonymously. Furthermore, the graphics and tables were created by the authors themselves and no third party has a claim to the illustrations. All methods used (analyses and training protocol) comply with the ethical and scientific standard of the Declaration of Helsinki and were reviewed and declared safe by the IST Ethics Committee. Furthermore, all methods used have been applied in previous research of our working group [41, 73, 74].

Ethical approval and informed consent

This study has been reviewed by the Local Ethics Committee of the IST University of Applied Sciences, Düsseldorf, Germany and has a positive ethical vote (02/2021). In addition, it would be registered in the German registry for clinical studies. All participants had to sign a written informed consent form before the start of the study (05/03/2021; DRKS00023826).

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Publisher's Note

Effects of endurance training on thyroid response in pre- and postmenopausal women

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Abstract

Purpose: Age-related changes in thyroid function are well investigated. Likewise, influences of physical activity on the thyroid gland could be determined. Studies that investigated the influence of (endurance) training on thyroid function in postmenopausal women are not existing. Therefore, this pilot study first examines thyroid hormone release after acute endurance training in pre- and postmenopausal women and second explores the impact of endurance intervention on thyroid function in postmenopausal women.

Methods: 12 pre- and 12 postmenopausal women were included. In all subjects, height, weight and body composition were assessed. TSH, fT4 and fT3 were assessed at 9:00 am and 9:40 am at rest and after an acute endurance exercise. Subsequently the postmenopausal women conducted a six-week walking intervention and repeated the tests.

Results: Weight, BMI and muscle mass was significantly lower and fat mass significantly higher in postmenopausal women ($p<.05$). Fat mass decreased and muscle mass increased ($p<.05$) in postmenopausal women after intervention. An elevated TSH response was found significantly in premenopausal women ($p=.028$) and non-significantly in postmenopausal women ($p=.135$) after acute exercise. There were no changes in fT3 and fT4 in both groups. After intervention postmenopausal women showed a significant reduction in fT3 response ($p=.015$) and a non-significant reduction of TSH response ($p=.432$).

Conclusion: This study provides evidence that both pre- and postmenopausal women respond with thyroid stimulation to acute endurance training. Furthermore this study provides preliminary evidence that an endurance training intervention can reduce thyroid response after acute endurance exercise in postmenopausal women.

Keywords: thyroid response, thyroid hormones, endurance exercise, postmenopausal women, premenopausal women

Statements and Declarations

Competing Interests: The authors have no conflict of interest.

Ethical approval: The study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the German Sports University Cologne (No 130/2019).

Informed concent: All participants read and signed the informed consent.

Introduction

Demographic change and the aging population poses new challenges for society and the healthcare system. Diseases occur more frequently in old age - thyroid function disorders included. The incidence of most thyroid diseases (hypothyroidism, nodular goiter, and cancer) is highest in postmenopausal and elderly women [1]. In this patient group, the diagnosis of thyroid dysfunction is difficult because symptoms may be nonspecific or co-occur with menopausal and aging symptoms [1]. In general, many age-specific changes in the thyroid gland and its functionality can be observed.

Histological changes in aging include an increase in interfollicular fibrosis, reduction in follicle size, flattening of glandular epithelial cells [2–4] and a decrease in overall weight of the thyroid gland [1–5]. In addition, neoplastic lesions increase, making the thyroid gland more nodular [1,5]. Observations conducted in iodine-rich areas have shown that serum TSH concentrations increase with age in both men and women. These observations may indicate decreased pituitary sensitivity to T4 in the aging population [6]. In addition, with increasing age, the ability of the thyroid gland to absorb iodine decreases and is 40% lower in people over 80 years of age than in individuals in their 30s [3]. Daily production of T4 decreases by 20 μg, but at the same time its metabolism slows down due to decreased activity of 5'-deiodinase-I. As a result, T4 half-life increases from 8 to 9.3 days and serum T4 concentration does not change during life [3]. Serum T3 and fT3 levels decrease with age [4,7] likely due to a decrease in peripheral T4-T3 conversion, which may contribute to decreased T4 depletion [7].

Physical activity could be one way to influence thyroid function in a targeted manner. However, the data on this issue are controversial. Several studies found no effect on blood TSH levels [8,9], while others found that TSH increases progressively during high-intensity exercise [9–11]. In addition, intensity dependent increases in T4 [8,10,12,13] and T3 [8,13] as well as decreases in T4 [12,13] and T3 [10,14] were observed as a result of endurance training. Studies that investigated the influence of (endurance) training on thyroid function in postmenopausal women are currently not existing.

Therefore, this study investigates to what extent the release of the hormones TSH, fT4 and fT3 can be stimulated by acute endurance exercise in pre- and postmenopausal women and to what extent the release of the thyroid hormones can be influenced by systematic endurance training in postmenopausal women. In addition, the extent to which body composition differs between premenopausal and postmenopausal women will be examined.

Methods

The pilot study included 12 untrained pre- and 12 untrained postmenopausal women. Recruitment was done via gynecologists, fitness studios, personal contacts and the German Menopause Society. Prior to recruitment start, the positive ethical approval of the ethics committee of the German Sport University Cologne (number 130/2019) was obtained and the study was registered in the German Clinical Trials Register (DRKS-ID: DRKS00020425). The study protocol is in accord with the Declaration of Helsinki. The inclusion and exclusion criteria are shown in Table 1.

Table 1: Inclusion and exclusion criteria

	Premenopausal women	**Postmenopausal women**
Inclusion criteria	18-30 years Regular menstrual cycle	50-65 years

Exclusion criteria	≥ 2 times endurance training per week Unbalanced diets (e.g. vegan) Hormone substitution (incl. oral contraceptives) Hormonal diseases Cardiac arrhythmias requiring treatment Metabolic diseases Heart failure (EF < 55) Performance-limiting pAVK (Fontaine stage ≥ II) Performance-limiting respiratory diseases Performance-limiting degenerative diseases Performance-limiting muscular diseases Performance-limiting renal diseases Performance-limiting neurological diseases Psychiatric and/or addictive diseases Performance-limiting oncological diseases in history (< 5 years)

The 12 premenopausal women completed 2 examination days at the German Sport University Cologne (trial A, B and C). The 12 postmenopausal women first completed 3 examination days (trial A, B and C), then completed a 6 week endurance training intervention and finally repeated the examinations (trial D, E and F). For organizational reasons, trials A and B or D and E were performed on one measuring day.

To exclude menstrual cycle-related influences of premenopausal women on thyroid hormones, examinations were performed in the second half (lutheal phase) of the subjects' menstrual cycle. Hormonal contraceptives were excluded. To confirm if the postmenopausal subjects were truly postmenopausal, the hormones estradiol and FSH were determined. Hormone replacement therapy (HRT) was excluded. The time schedule is shown in Fig. 1.

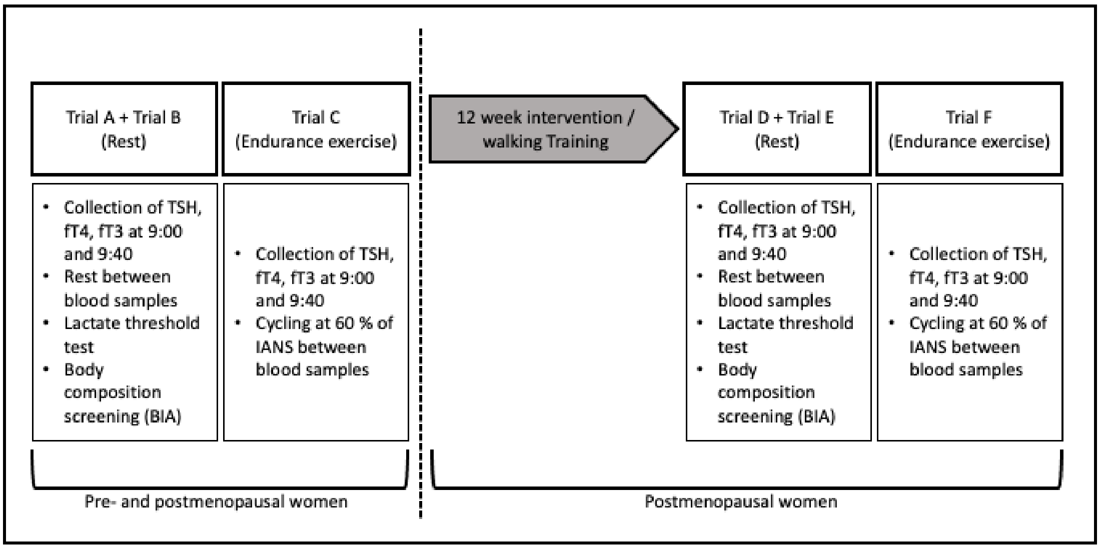


Fig. 1: Time schedule

Trials A and D

After informed consent was obtained and signed (only trial A), anthropometric data were collected and body composition was measured by bio-impedance analysis (BodyExplorer, Kommunikation & Service GmbH).

Trials B and E

Subjects appeared fasting. Two blood tests were taken at 9:00 am (t0) and at 9:40 am (t1) to identify female sex hormones (Estradiol, FSH) as well as circadian changes in thyroid hormones (TSH, fT4, fT3) without exercise. For the identification of the individual anaerobic threshold, an endurance threshold test was performed on a bicycle ergometer (ergoselect 50, Typ: optibike med K ergoline) according to the WHO scheme. Heart rate was monitored via watch with chest belt (Sigma PC 15).

Trials C and F

As on the previous day, participants appeared fasting and blood draws were performed at 9:00 am and 9:40 am. Between blood draws (30 minutes), exercise was performed on a bicycle ergometer at 60% - 65% of the individual anaerobic threshold.

Intervention of postmenopausal women

After examinations A-C, the postmenopausal women started into a six-week intervention phase. During the intervention, the subjects exercised three times per week for 45 minutes. In order to offer a standardized form of training the subjects conducted a walking training with heart rate monitors. The training was controlled by pulse rate watches and the BORG scale. All training units were performed at pulse values of 55% - 70% of maxHR and/or with BORG values between 11 and 14. The participants had to record their training sessions in a training diary with date, heart rate and BORG value. All training units were performed in the form of a continuous load. The intervention was supervised via e-mail and/or telephone contact to ensure a suitable intensity and to be able to react to possible complications.

Data analysis

For statistical analysis the IBM SPSS Statistics 28 program was used. The Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to determine the normal distribution. In case of different results, the Shapiro-Wilk test was used, since it has a higher test strength [15,16]. If the distribution was normal, the t-test was used; if it was not, the Mann-Whitney U-test or the Wilcoxon test was used.

Results

Body composition: differences of pre- and postmenopausal women

BMI differs significantly between pre- and postmenopausal women. Postmenopausal women showed an average BMI value of 3.39 points higher than premenopausal women.

A highly significant difference was found in terms of skeletal muscle mass in kg and % between pre- and postmenopausal women. Muscle mass was 3.13 kg higher in premenopausal women than in postmenopausal women ($U=13.00$, $Z=-3.120$, $p=.001$), using the exact sampling distribution of U, $r=-.66$. In premenopausal women muscle mass was 9.37% higher than in postmenopausal women (95%-CI[6.17,12.57], $t(20)=6.10$, $p<.001$, $d=2.6$).

Fat mass in kg differs highly significantly between pre- and postmenopausal women. It was higher in postmenopausal women than in premenopausal women by an average of 8.99 kg (95% CI[-14.67,-3.33], $t(20)=-3.31$, $p=.003$, $d=-1.4$). Fat mass in % showed a highly significant difference. It was in postmenopausal women by an average of 8.73% higher than in premenopausal women (95%-CI[- 14.87,-2.60], $t(20)=-2.97$, $p=.008$, $d=-1.3$).

Body composition: differences of postmenopausal women before and after intervention

There was no significant difference in weight ($t(11)=-.42$, $p=.686$, $d=.12$) and BMI ($t(11)=-.58$, $p=.571$, $d=.17$) of postmenopausal women before and after intervention. There was a significant difference in skeletal muscle mass before and after intervention. Muscle mass was on average 1.71 kg higher ($t(10)=-3.02$, $p=.013$, $d=.91$) and the percentage of muscle mass was on average 1.38% higher after the intervention ($t(10)=-2.79$, $p=.019$, $d=-.84$). Fat mass also changed significantly through training intervention, decreasing by 0.13 kg (t(10)=2.42, p=.036, d=.73) or 1.77% (t(10)=2.57, p=.028, d=.78).

Table 2: Age and body composition

	Premenopausal *Baseline*	Postmenopausal *Baseline / Pre-Intervention*	Postmenopausal *Post-Intervention*
Age	24 ± 2,41*[1]	57 ± 3,47*[1]	/
BMI	21,45 ± 1,40*[1]	24,83 ± 3,99*[1]	24,89 ± 4,14
Weight (kg)	60 ± 5,16*[1]	70,54 ± 11,38*[1]	70,67 ± 11,70
Fat mass (kg)	16,32 ±4,57*[1]	25,31 ± 7,28*[1] *[2]	25,18 ± 8,11*[2]
Fat mass (%)	27,61 ± 7,19*[1]	36,34 ± 5,90*[1] *[2]	34,57 ± 6,67*[2]
Muscle mass (kg)	21,09 ±2,26*[1]	17,96 ± 2,05*[1] *[2]	19,67 ± 3,10*[2]
Muscle mass (%)	35,90 ± 3,43*[1]	26,53 ± 3,44*[1] *[2]	27,91 ± 4,41*[2]

*[1] sig. difference (p < 0.05) between pre- and postmenopausal women at baseline

*[2] sig. difference (p < 0.05) between postmenopausal women before and after intervention

Thyroid hormone response: Pre-Intervention

Thyroid hormone response was defined as the difference of hormone concentrations between timepoint t1 and t0.

At baseline, the results showed no significant difference between pre- and postmenopausal women for fT4 (p=.736, 95% CI[-.11,.09], t(22),-.17, p=.863, d=0.07) TSH (p=.145, 95%-CI[-.74,.98], t(22),.29, p=.777, d=.12) and fT3 (U=68.00, Z=-.234, p=.830).

Considering the thyroid response (= difference of TSH, fT4 and fT3 concentration between the second and the first blood sample of an examination day) between the "rest" and "exercise" condition, there was a significant difference in TSH in premenopausal women (t(11)=2.53, p=.028, d=.73) and non-significant differences in fT4 (Z=-.816, p=.688, r=0.23) and fT3 (Z=-1.046, p=.313, r= 0.30). In the group of postmenopausal women, there was no significant difference in fT3 (t(11)=-2.15, p=.054, d=.62), fT4 (Z=-.632, p=.766, r=.18) and TSH response (Z=-1.531, p=.135, r=.44).

There was no significant difference in thyroid response of fT4 (U=61.50, Z=-.730, p=.552), fT3 (U=63.00, Z=-.552, p=.618) and TSH (U=68.00, Z=-.231, p=.832) between pre- and postmenopausal women in the “rest” condition. There was also no significant difference of the thyroid response between pre- and postmenopausal women in the "exercise" condition for fT4 (U=66.50, Z=-.448, p=.832), fT3 (U=63.00, Z=-.545, p=.614), and TSH (U=56.50, Z=-.895, p=.385).

Thyroid hormone response: Post-Intervention

Comparing the "rest" conditions before and after training intervention of the postmenopausal women, no significant differences in thyroid hormone response were found (fT3, t(11)=1.59, p=.139, d=.46.; fT4, Z=-.541, p=.781, r=.16; TSH, Z=-1.452, p=.157, r=.42). Likewise, comparing the "exercise" conditions before and after training intervention, no significant differences in thyroid hormone response were found (fT3, t(11)=.48, p=.638, d=.14; fT4 , Z=-1.000, p=.531, r=.29; TSH, Z=-.981, p=.349, r=.28.).

There was no significant difference in thyroid hormone response between “rest” and “exercise” in postmenopausal women after intervention of fT4 (Z=-1.725, p=.125, r=.50). There was a significant difference between rest and exercise in postmenopausal women after intervention in fT3 response (t(11)=-2. 87, p=.015, d=.83), with fT3 levels decreasing by 0.1 pg/ml after acute exercise. No significant difference was seen between rest and exercise in postmenopausal women in TSH response (t(11)=.82, p=.432, d=.23).

Table 3: Thyroid hormone concentration

Pre-Intervention	TSH rest		TSH stress		fT4 rest		fT4 stress		fT3 rest		fT3 stress	
	T0	**T1**	**T0**	**T1**	**T0**	**T1**	**T0**	**T1**	**T0**	**T1**	**T0**	**T1**
Premenopausal women (n=12)	2,1± 0,85	1,81 ± 0,65	1,65 ± 0,61	1,52 ± 0,53	1,18 ± 0,11	1,18 ± 0,08	1,19 ± 0,10	1,18 ± 0,12	3,42 ± 0,36	3,38 ± 0,36	3,38 ± 0,32	3,3 ± 0,29
Postmenopausal women (n=12)	1,92 ± 1,09	1,79 ± 0,87	1,65 ± 0,74	1,65 ± 0,79	1,18 ± 0,11	1,2 ± 0,12	1,18 ± 0,09	1,17 ± 0,11	3,33 ± 0,22	3,29 ± 0,22	3,26 ± 0,26	3,15 ± 0,22
Post-Intervention	**TSH rest**		**TSH stress**		**fT4 rest**		**fT4 stress**		**fT3 rest**		**fT3 stress**	
	T0	**T1**	**T0**	**T1**	**T0**	**T1**	**T0**	**T1**	**T0**	**T1**	**T0**	**T1**
Postmenopausal women (n=12)	1,92 ± 0,91	1,73 ± 0,86	1,95 ± 0,80	1,80 ± 0,73	1,11 ± 0,13	1,14 ± 0,10	1,12 ± 0,11	1,08 ± 0,13	3,15 ± 0,28	3,17 ± 0,26	3,18 ± 0,27	3,1 ± 0,28

Annotation: There were no significant within-group differences and no significant group differences of hormone concentrations ($p > .05$)

Table 4: Thyroid hormone response

Pre-Intervention	TSH rest	TSH stress	fT4 rest	fT4 stress	fT3 rest	fT3 stress
Premenopausal women (n=12)	-0,30 ± 0,28*[1]	-0,13 ± 0,19*[1]	0,01 ± 0,13	-0,01 ± 0,05	-0,03 ± 0,13	-0,08 ± 0,10
Postmenopausal women (n=12)	-0,20 ± 0,56	-0,02 ± 0,31	0,02 ± 0,08	0 ± 0,04	-0,03 ± 0,09	-0,1 ± 0,09
Post-Intervention	**TSH rest**	**TSH stress**	**fT4 rest**	**fT4 stress**	**fT3 rest**	**fT3 stress**
Postmenopausal women (n=12)	-0,19 ± 0,17	-0,15 ± 0,1	0,03 ± 0,09	-0,03 ± 0,10	0,02 ± 0,10*[2]	-0,08 ± 0,13*[2]

Annotation: Thyroid hormone response was defined as the difference between timepoint t1 and t0

*[1] Comparison between premenopausal women at rest and after exercise: $p < 0.05$

*[2] Comparison between postmenopausal women at rest and after exercise (post-intervention): $p < 0.05$

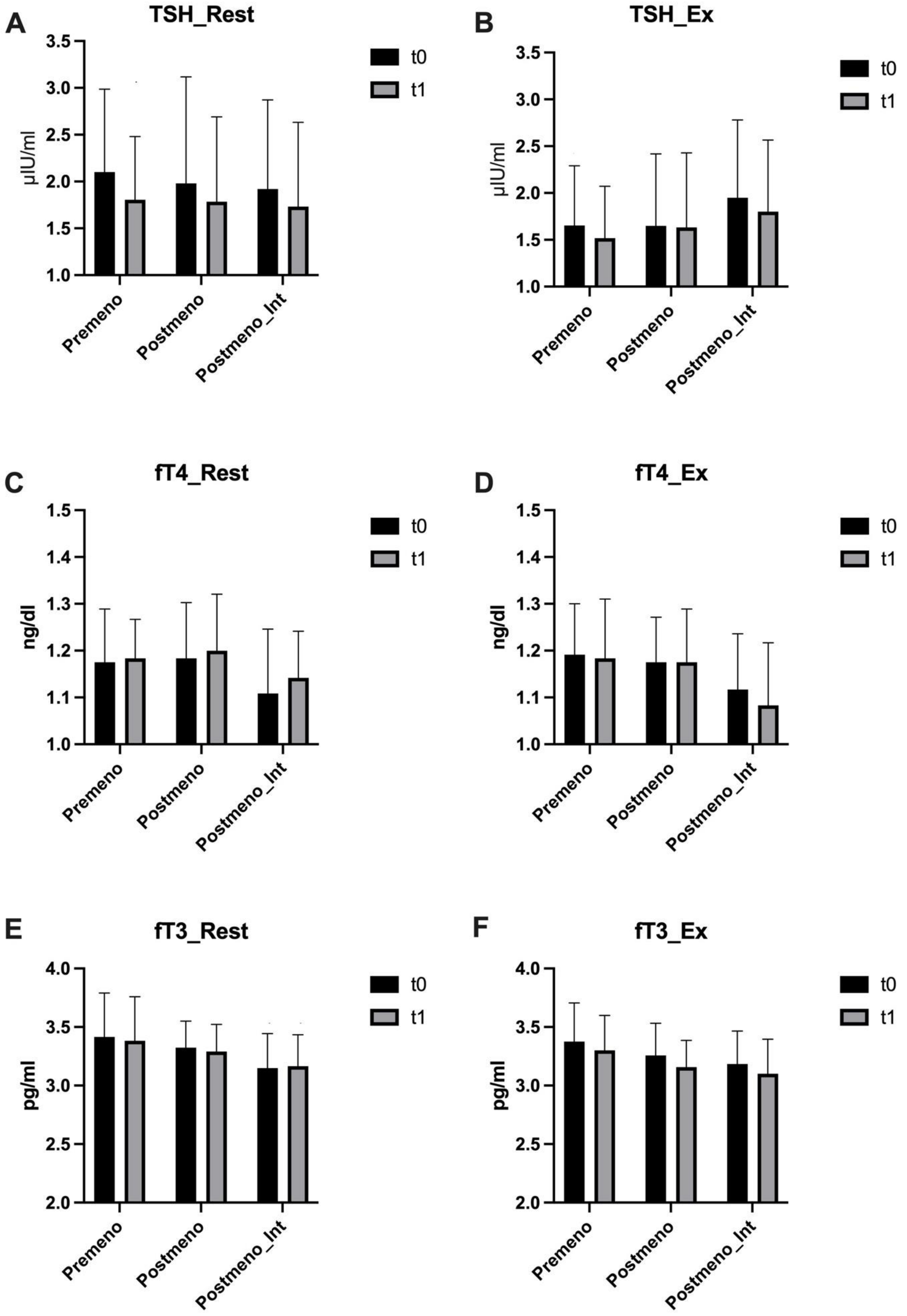
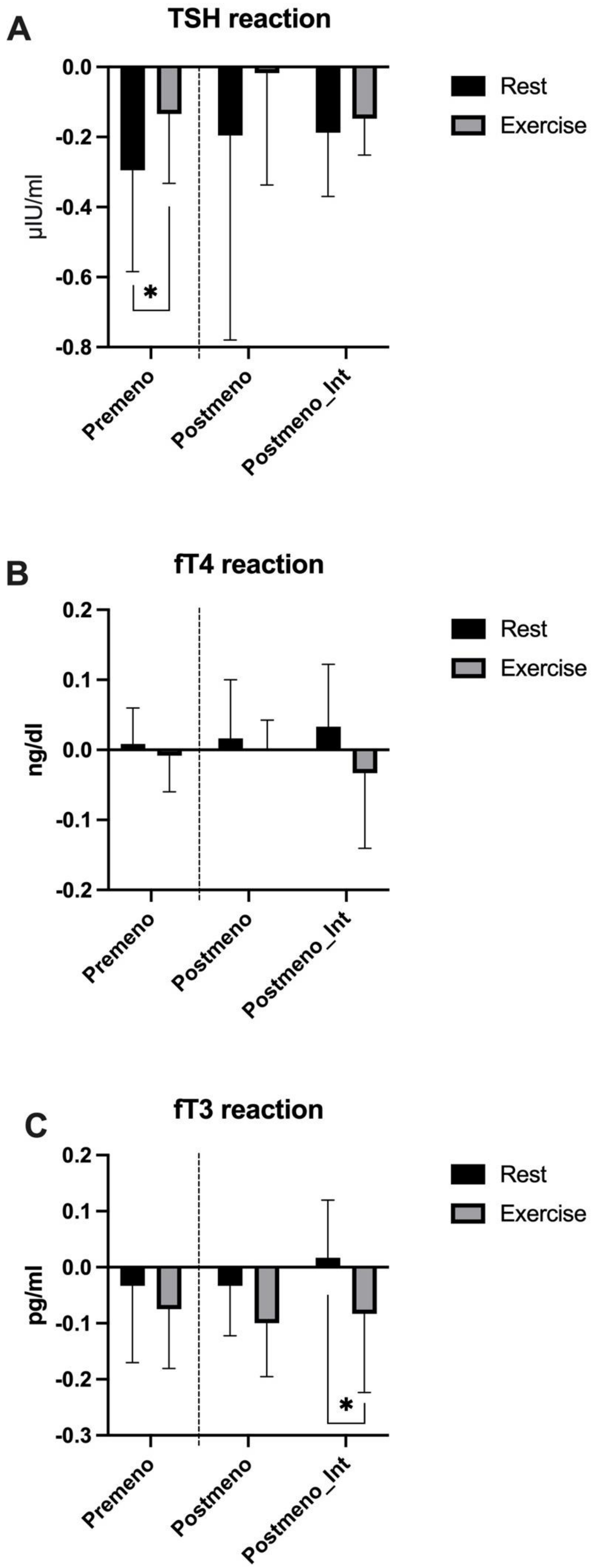


Fig. 2: Thyroid hormone concentration

(Rest = no training between 9:00 and 9:40; Ex = acute endurance exercise between 9:00 and 9:40)


A
TSH reaction
µIU/ml
0.0
-0.2
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Premeno
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Premeno
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0.2
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Exercise

Fig. 3: Thyroid hormone response

Discussion

In our study, we first investigated to what extent body composition differs between pre- and postmenopausal women and observed to what extent the thyroid gland can be stimulated in pre- and postmenopausal women by acute aerobic exercise. Second, we examined the extent to which the body composition of postmenopausal women is changed by 6 weeks of endurance training and whether thyroid response can be altered by an endurance intervention.

Body composition

It was found that the premenopausal women had lower BMI, lower body weight, more muscle mass and lower body fat in comparison with the postmenopausal women. These results are consistent with findings from other studies [17–19]. A possible molecular mechanism discussed is an estrogen related change in the fat metabolism of postmenopausal women [20]. In animal experiments [21,22] as well as in human intervention studies [23] it could be demonstrated that fat metabolism is directly influenced by 17 beta-estradiol. Although hormone replacement therapy with estradiol can positively influence lean body mass initially (within the first 3 years), the effects are regressive in the long term [24]. Therefore, physical activity is an important measure to reduce the age-related reduction of lean body mass in the long term.

The six-week endurance training greatly improved the body composition of the postmenopausal women through a significant increase in muscle mass and a significant reduction in fat mass. The significant increase in muscle mass due to endurance training is particularly remarkable and can be explained by the fact that the postmenopausal women were untrained - therefore not exercising at all or not exercising regularly. It has already been proven that untrained elderly subjects can build muscle mass through systematic endurance training [25].

Thyroid hormone response

At baseline, no differences in hormone concentrations of TSH, fT4, and fT3 were detected between premenopausal and postmenopausal women. It is known that TSH concentrations increase with age [26–28], by about 5-10 μIU/ml every decade [26]. However, this could not be shown in our study. Presumably, this was due to the small sample size.

Furthermore, in premenopausal women a significant elevated TSH response and therefore an increased stimulation of the thyroid gland could be induced by endurance training. The postmenopausal women react with a non-significant increased TSH response due to acute endurance exercise. Since changes in TSH are descriptively detectable, it can be assumed that the sample was too small to identify significant changes in TSH in postmenopausal women. In other studies, it has already been shown that endurance training can increase the TSH concentration [10,11,13]. Regarding the hormones fT3 and fT4, no changes could be detected in both groups. The data suggest that both pre- and postmenopausal women respond to acute aerobic exercise by increased TSH release due to greater thyroid hormone demand.

Through training intervention no significant change in TSH response of the postmenopausal women could be detected. Nevertheless, descriptively, a greater decrease in TSH or a weaker TSH response after acute exercise was observed in comparison of pre- and post-intervention measurements. Furthermore, postmenopausal women showed a significantly reduced fT3 response by acute, aerobic exercise after the training intervention compared with the resting condition. The data regarding the response of acute exercise on thyroid hormone concentrations is controversial. Some previous studies assessing thyroid hormones after exercise found increased concentrations of TSH, T4 and T3 [11,13]. Other studies, noted a decrease in thyroid hormones [10,29]. The biological effects of short term changes in thyroid hormone concentrations are not fully understood, although they may be important in the body's adaptation to stressful or catabolic states [30,31].

However, in this study, it can be assumed that the intervention-induced adaptations of the postmenopausal women resulted in the need for a lower release of thyroid hormones. Indications suggesting a reduced thyroid response in postmenopausal women (post-intervention) are a greater - although not significant - decrease in TSH concentration after acute stress as well as a significantly reduced fT3 release. In animal model, it has already been demonstrated that an endurance training intervention can lead to a greater amount of thyroid hormone receptors [32,33]. As a result, a lower concentration of thyroid hormones could lead to higher metabolism-increasing effects in target tissues. However, these effects have to be confirmed in humans. In addition, the intervention is likely to improve women's intra- and intermuscular coordination. Therefore, it is expected that acute endurance exercise was experienced as less intense due to increased exercise efficiency and improved muscle activation. As a result, a reduced activation of metabolism is necessary and therefore a reduced release of thyroid hormones.

Limitations

The number of subjects in this study was low, with n = 12 per group. For this reason, potential changes may not have become evident. Furthermore, the intervention duration of six weeks may have been too short to make all training-related changes visible. Nevertheless, changes could already be observed after six weeks. Another point to be considered in the interpretation is the determination of the training heart rate for the walking intervention by a load test on the bicycle ergometer. This could result in an underestimation of the subjects' performance.

Conclusion

In summary, a difference in body composition was found between the pre- and postmenopausal women. The premenopausal women showed significantly lower weight, BMI and body fat as well as significantly higher muscle mass. However, with six weeks of endurance training, the fat mass of the postmenopausal women can be reduced and their muscle mass increased. In addition, both pre- and postmenopausal women respond to acute aerobic exercise with an enhanced thyroid response through an elevated TSH secretion. After a six-week exercise intervention of the postmenopausal women, a non-significantly decreased response of TSH after acute endurance exercise was demonstrated as well as a significantly reduced fT3 response.

Therefore, this study provides preliminary evidence that endurance training reduces the thyroid response of postmenopausal women after acute exercise. Whether the reduced need for thyroid hormones after stress is clinically relevant remains to be verified in future studies. However, the results point to the hypothesis that possibly patients with mild, subclinical hypothyroidism might benefit from targeted endurance training in terms of symptom relief or possible reduced doses of thyroxine. Further studies are needed to explore this hypothesis.

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