

UNIVERSIDADE EVANGÉLICA DE GOIÁS
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DO MOVIMENTO
HUMANO E REABILITAÇÃO

KATIELLE RODRIGUES DA SILVA CARDOSO

**ANÁLISE DE REPRODUTIBILIDADE E REPETIBILIDADE EM
MEDIDAS DE ÁREA DE SECÇÃO TRANSVERSAL MUSCU-
LAR COM ULTRASSONOGRRAFIA: UM ESTUDO DE
AVALIAÇÃO INTERDIAS E INTRA/INTER AVALIADORES**

Anápolis – GO

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RESUMO

Hipertrofia muscular é definida como o aumento da massa muscular total. Toda hipertrofia muscular resulta no aumento do número de filamentos de actina e miosina em cada fibra muscular. O músculo esquelético é plástico, em parte, há um equilíbrio entre a síntese proteica e a degradação proteica. A exposição do músculo esquelético ao estímulo do treinamento físico gera adaptações, como força e hipertrofia (síntese proteica), ao ponto que a inatividade gera à atrofia muscular (degradação proteica). Desde os seus primeiros relatos na literatura, imagens de cortes anatómicos vêm sendo utilizados com a finalidade de avaliar o tecido muscular com um alto grau de precisão e confiabilidade através de procedimentos tal como a ressonância magnética (RM), que permite uma avaliação precisa sobre o tecido muscular, desde análise de áreas de secção transversa (AST), ou com a finalidade de diagnosticar lesões musculares. Porém seu uso se limita a ambientes laboratoriais tornando-se um procedimento o tanto quanto inviável para medição em ambientes clínicos, além de seu alto custo. Portanto se fez necessário o uso de novas técnicas e ferramentas com a finalidade de identificar imagens de áreas musculares que apresentem um alto grau de validade e acessíveis. Uma ferramenta que vem sendo explorada dentro de ambientes clínicos é o aparelho de ultrassonografia que é capaz de gerar imagens de grupamentos musculares. Objetivos. Determinar a validade de medidas de ultrassonografia, intra e entre avaliadores, com um coeficiente de correlação sobre a espessura muscular do reto femoral. Métodos. A amostra para o estudo de reprodutibilidade foi estabelecida considerando os testes a serem realizados (correlação interclasse), poder de 80%, tamanho de efeito médio de 0,5, nível e significância 5% sendo necessários 52 participantes. Para a análise de repetibilidade foi usado o software G*Power (versão 3.0), considerada a coleta com dois grupos e três medidas do mesmo participante (ANOVA para medidas repetidas) para cada grupo, poder de 95%, tamanho de efeito médio (f) de 0,25, nível e significância 5% e perdas de 20% sendo necessários 86 participantes. A ultrassonografia Mindray modelo M6 irá ser usada para determinar a espessura do músculo reto femoral (RF) usando uma sonda linear com frequência de 6-14 mega-hertz (MHz) modelo L14-6Ns. Foram adotados os pontos anatómicos do fêmur da coxa direita, em seguida o posicionamento de 40% do comprimento do fêmur para a região proximal para a análise de espessura do músculo reto femoral (RF). Antes do início do experimento foram feitas marcações sobre a pele com uma fita crepe afim de padronizar as distancias entre os pontos anatómicos que serviram de referência para o posicionamento da sonda, todas as medidas foram realizadas sobre o membro direito dos avaliados, para a obtenção das imagens os sujeitos se posicionaram em decúbito dorsal sobre uma maca com as pernas totalmente estendidas e seus músculos relaxados durante um período cronometrado de 10 minutos, durante o processo foi aplicado uma generosa quantidade de gel solúvel em água de contato que será aplicada de forma direta sobre o transdutor afim de minimizar a distorção das imagens e auxiliar no acoplamento acústico. Todas as visitas foram realizadas no mesmo local climatizado o qual contou com a presença de um profissional afim de assegurar a validade dos procedimentos acima listados.

Palavras Chave: hipertrofia muscular; ultrassonografia; reprodutibilidade; secção transversa muscular;

Abstract

Introduction. Muscle hypertrophy is defined as an increase in total muscle mass. All muscle hypertrophy results in an increase in the number of actin and myosin filaments in each muscle fiber. Skeletal muscle is plastic, in part, there is a balance between protein synthesis and protein breakdown. The exposure of skeletal muscle to the stimulus of physical training generates adaptations, such as strength and hypertrophy (protein synthesis), to the point that inactivity generates muscle atrophy (protein degradation). Since its first reports in the literature, images of anatomical sections have been used with the purpose of evaluating muscle tissue with a high degree of precision and reliability through procedures such as magnetic resonance imaging (rm), which allows an accurate assessment of the muscle tissue, from analysis of cross-sectional areas, or for the purpose of diagnosing muscle injuries. However, its use is limited to laboratory environments, making it a procedure that is as unfeasible for measurement in clinical environments, in addition to its high cost. Therefore, it was necessary to use new techniques and tools in order to identify images of muscle areas that have a high degree of validity and are accessible. A tool that has been explored within clinical environments is the ultrasound device that is capable of generating images of muscle groups.

Objective. To determine the validity of intra- and inter-rater ultrasound measurements with a correlation coefficient on rectus femoris muscle thickness.

Methods. The sample for the reproducibility study was established considering the tests to be performed (interclass correlation), power of 80%, average effect size of 0.5, level and significance of 5%, requiring 52 participants. For the repeatability analysis, the G*Power software (version 3.0) was used, considering the collection with two groups and three measurements from the same participant (ANOVA for repeated measures) for each group, power of 95%, average effect size (f) of 0.25, level and significance of 5% and losses of 20%, requiring 86 participants. Mindray model M6 ultrasonography will be used to determine rectus femoris (RF) muscle thickness using a linear probe with a frequency of 6-14 megahertz (MHz) model L14-6Ns. The anatomical points of the femur of the right thigh were adopted, followed by the positioning of 40% of the length of the femur towards the proximal region for the analysis of the thickness of the rectus femoris (RF) muscle. Before the beginning of the experiment, marks will be made on the skin with a masking tape in order to standardize the distances between the anatomical points that will serve as a reference for the positioning of the probe, all measurements will be carried out on the right limb of the evaluated ones, to obtain of the images, the subjects will position themselves in dorsal decubitus on a stretcher with their legs fully extended and their muscles relaxed during a timed period of 10 minutes, during the process a generous amount of gel soluble in contact water will be applied that will be applied directly over the transducer in order to minimize image distortion and assist in acoustic coupling. All visits will be carried out at the same in an air-conditioned place, which will be attended by a professional in order to ensure the validity of the procedures listed above.

Keywords: muscle hypertrophy; ultrasound; reproducibility; muscle cross section;

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LISTA DE SIGLAS E ABREVIATURAS

AST - áreas de secção transversa

RM - ressonância magnética

RF - reto femoral

MHz - mega-hertz

SR - retículo sarcoplasmático

HM - hipertermia maligna

DCC - doença do núcleo central

G - Coeficientes de generalização

CCI - coeficientes de correlação intra examinadores

ERM - erro padrão de medida

ETM - erro típico da medida

EM - espessura muscular

ICC - coeficiente de correlação intraclasse

1- INTRODUÇÃO

Em Seres Humanos, a massa muscular permanece relativamente estável durante o início da vida, mas após os 30 anos de idade, inicia-se um processo natural de redução de massa muscular a uma taxa de 0,5 a 1,0% ao ano¹. Com o processo de envelhecimento, o equilíbrio prejudicado entre a síntese proteica e a proteólise no músculo esquelético resulta em um declínio progressivo na massa, força e função do músculo esquelético e é definido como sarcopenia². À medida que a força dos músculos dos membros e dos músculos respiratórios diminui gradualmente, as funções e atividades físicas normais, como respirar, ficar em pé, andar e correr, também diminuirão¹. Em média, o pico de força diminui em 20-40% entre 30 e 80 anos. A perda de massa muscular resulta em sérias consequências e diversas doenças crônicas e senilidade, caracterizada por perdas funcionais, fraqueza muscular, perda de independência e aumento do risco de quedas e de morte³.

Até o momento, a atividade física, com foco na resistência (força) treinamento, é endossado como uma terapia de primeira linha para gerenciar a sarcopenia⁴. Estudos clínicos randomizados e controlados mostraram efeitos positivos do treinamento de resistência em massa muscular, força muscular e desempenho físico^{5,6}.

O ganho de força e massa muscular é um processo complexo que envolve vários fatores, incluindo o treinamento de força, a nutrição adequada e o descanso suficiente⁷. O treinamento de força é uma das formas mais eficazes de aumentar a força e a massa muscular⁷. Ele envolve o uso de pesos livres, máquinas de musculação ou o peso do próprio corpo para sobrecarregar os músculos e estimular o crescimento muscular⁷. O treinamento de força deve ser progressivo e desafiador para maximizar o ganho de força e massa muscular⁷.

A nutrição adequada é essencial para o ganho de força e massa muscular. A ingestão de proteínas é especialmente importante, pois as proteínas são os blocos de construção dos músculos⁸. A quantidade de proteína necessária varia de acordo com o indivíduo e o nível de atividade física, mas geralmente é recomendado consumir cerca de 1,6g de proteína por quilo de peso corporal por dia para maximizar o ganho de massa muscular⁹.

O descanso é outro fator importante no ganho de força e massa muscular. O músculo precisa de tempo para se recuperar e crescer após o treinamento de força¹⁰.

Existem várias formas de aferir o ganho de massa muscular. Uma das formas mais comuns é medir a circunferência do músculo antes e depois do treinamento de força através da perimetria ¹¹. A densitometria óssea também pode ser usada para avaliar o ganho de massa muscular, pois a massa muscular está diretamente relacionada à densidade óssea ¹². Além disso, a bioimpedância elétrica é uma técnica não invasiva que pode ser usada para medir a composição corporal, incluindo a massa muscular. Outra forma é medir a espessura do músculo usando ultrassonografia ¹¹.

A área de seção transversa muscular é uma medida da área da superfície muscular que é cortada por um plano perpendicular ao eixo longitudinal do músculo. Ela é frequentemente usada para avaliar a força muscular e a hipertrofia muscular. A área de seção transversa muscular pode ser calculada por meio de várias técnicas, como ultrassonografia, ressonância magnética e tomografia computadorizada ¹¹. A ultrassonografia é uma técnica não invasiva e amplamente utilizada para medir a área de seção transversa muscular ¹³. A ressonância magnética e a tomografia computadorizada são técnicas mais precisas, mas são mais caras e menos acessíveis ¹¹.

A área de seção transversa muscular é uma medida importante na avaliação da força muscular e da hipertrofia muscular. Ela é diretamente proporcional à força muscular, o que significa que quanto maior a área de seção transversa muscular, maior a força muscular. Além disso, a área de seção transversa muscular é um indicador da hipertrofia muscular, que é o aumento do tamanho das fibras musculares. A hipertrofia muscular é um processo adaptativo que ocorre em resposta ao treinamento de força e é um dos principais mecanismos responsáveis pelo aumento da força muscular¹⁴.

Resumidamente, o músculo esquelético é um tecido altamente organizado que contém vários feixes de fibras musculares (miofibras). Cada miofibrila (contendo várias miofibrilas), representa uma célula muscular com sua unidade celular básica chamada sarcômero. Pacotes de miofibras formam os fascículos e os feixes de fascículos formam o tecido muscular, com cada camada sucessivamente encapsulada por matriz extracelular ¹⁵ e apoiada pelas redes do citoesqueleto. O músculo esquelético é altamente vascularizado e innervado, e incorporado com componentes da maquinaria metabólica e reguladora, apoiando eficiência na produção de energia e homeostase celular. A atividade precisamente coordenada entre cada um desses

componentes é essencial para moldar o estado de saúde muscular e atividade motora associada. Quaisquer perturbações (por exemplo, genéticas ou ambientais) a esta coordenação, resultam em perda de saúde e função muscular, tipicamente caracterizada por perda de fibras musculares, redução do rendimento motor e, em alguns casos, morte.

A figura 01 ilustra a estrutura muscular clássica.

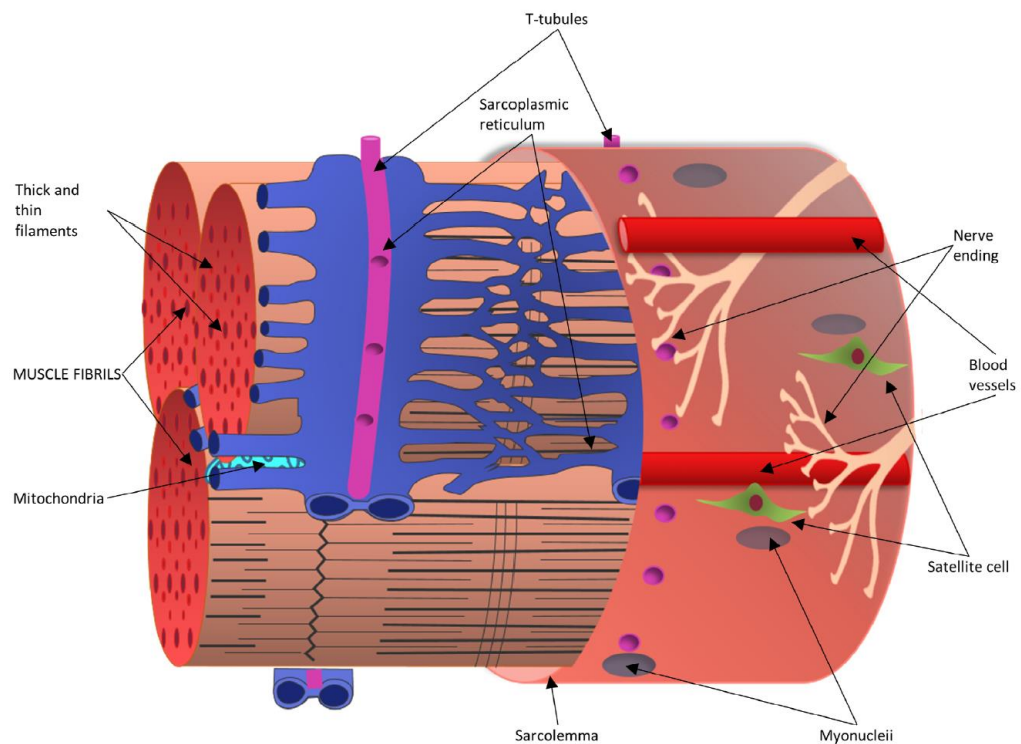


Figura 01: Representação esquemática da fibra muscular esquelética – uma única fibra muscular madura é mostrada aqui como um feixe de miofibrilas, encapsuladas pelo sarcolema. O retículo sarcoplasmático envolve fibrilas com túbulos transversos (T) que as cruzam. Feixes de miofibrilas formam fascículos, que se agrupam para formar o tecido muscular. As células satélites residem ao longo da fibra muscular hospedeira, diretamente acima do sarcolema, sob a lâmina basal do músculo e na proximidade dos mionúcleos. As fibras nervosas inervantes e os capilares locais estendem-se ao longo do comprimento da fibra muscular. Cada camada é sucessivamente envolvida pela matriz extracelular. **Fonte: Mukund & Subramaniann 2019.**

1.1- Contração Muscular

"A contração muscular é um processo complexo que se desenrola em diferentes etapas, desde o início até a execução. Vamos explorar essas etapas de forma mais detalhada: O processo começa com um estímulo nervoso. Quando o cérebro envia um sinal elétrico através dos nervos para o músculo, desencadeia uma reação. O impulso nervoso atinge a junção neuromuscular, o ponto de contato entre o nervo e o músculo. Aqui, ocorre a liberação de neurotransmissores, como a acetilcolina. A acetilcolina é liberada e se liga aos receptores na membrana da fibra muscu-

lar, desencadeando um novo impulso elétrico ao longo da fibra. O impulso elétrico percorre as fibras musculares por meio do sistema de túbulos T, desencadeando a liberação de íons de cálcio no interior da fibra muscular. A presença de íons de cálcio permite que as cabeças de miosina se unam às fibras de actina, iniciando o processo de contração muscular propriamente dito. Durante a contração, as cabeças de miosina formam pontes cruzadas com as fibras de actina, puxando-as mais próximas umas das outras. As pontes cruzadas se movem ao longo das fibras de actina, resultando no encurtamento da fibra muscular e, assim, na contração muscular.¹⁶

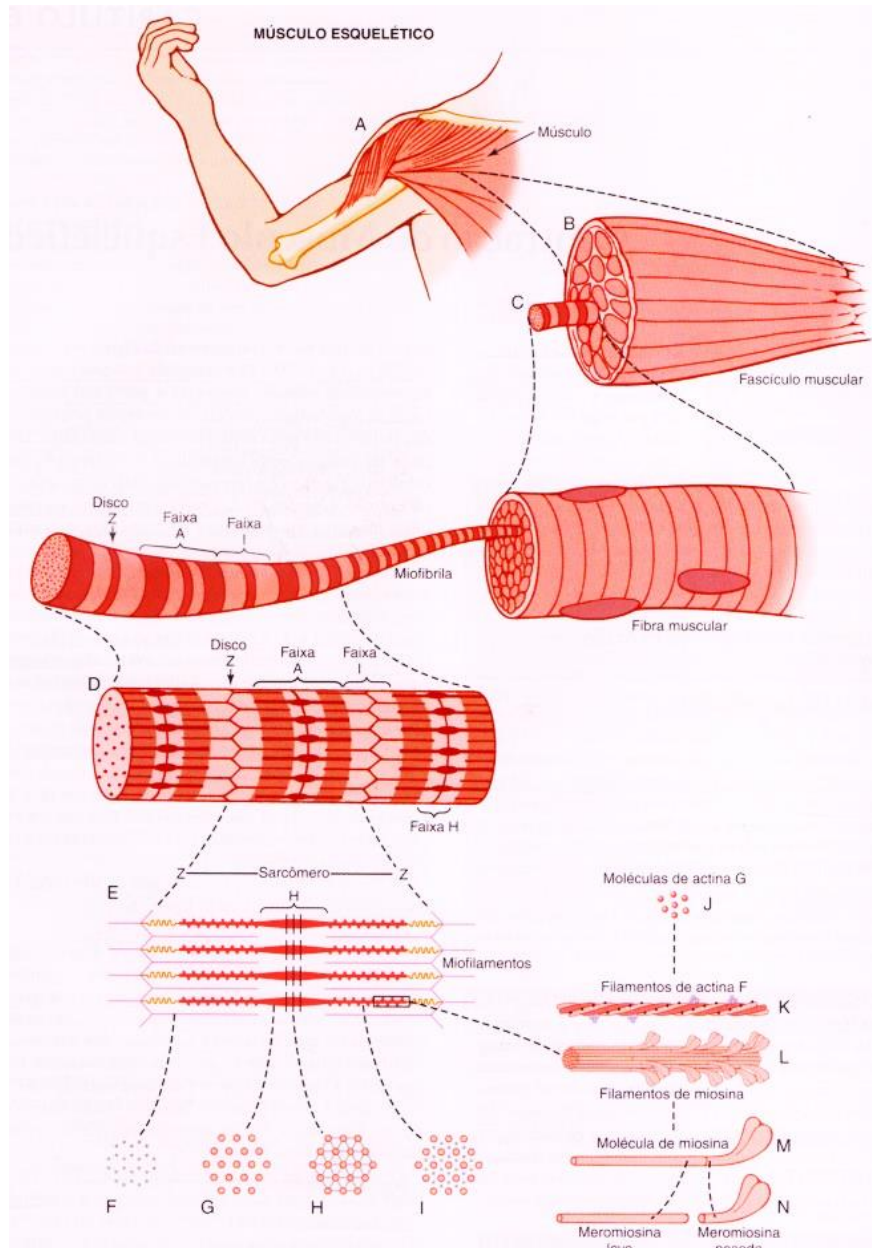


Figura 02: Organização do músculo esquelético do nível macroscópico ao molecular. Fonte:

(16)

1.2- GERAÇÃO DE FORÇA

A geração de força e o movimento rápido são características da função muscular estriada provocada pela contração do sarcômero. Os sarcômeros representam uma elegante peça de maquinaria molecular cuja estrutura complexa é composta por dois principais conjuntos de filamentos de proteínas: filamentos finos (α -actina e proteínas associadas) e filamentos grossos (miosina e proteínas associadas) que correm paralelamente ao eixo da fibra muscular. Visualmente, o sarcômero é delimitado em cada extremidade por uma linha estreita e escura chamada Zdisk. Cada disco Z divide uma banda I mais leve que é compartilhada entre sarcômeros adjacentes. No centro do sarcômero está uma banda A densa composta por filamentos grossos, com zona H mais clara. A linha M divide a zona H. Filamentos finos são mantidos juntos, em um arranjo lateral, no disco Z, enquanto a banda M interconecta os filamentos grossos (17). Funcionalmente, a contração começa com a ligação da troponina-C com o Ca^{2+} liberado durante o acoplamento excitação-contração (CEC). Isso provoca uma alteração de conformação no complexo troponina-tropomiosina resultando na exposição dos locais de ligação da miosina nos filamentos de actina. As cabeças de miosina então se ligam e rastejam ao longo do comprimento do filamento de actina, provocando a hidrólise do ATP e subsequentemente contração ¹⁸.

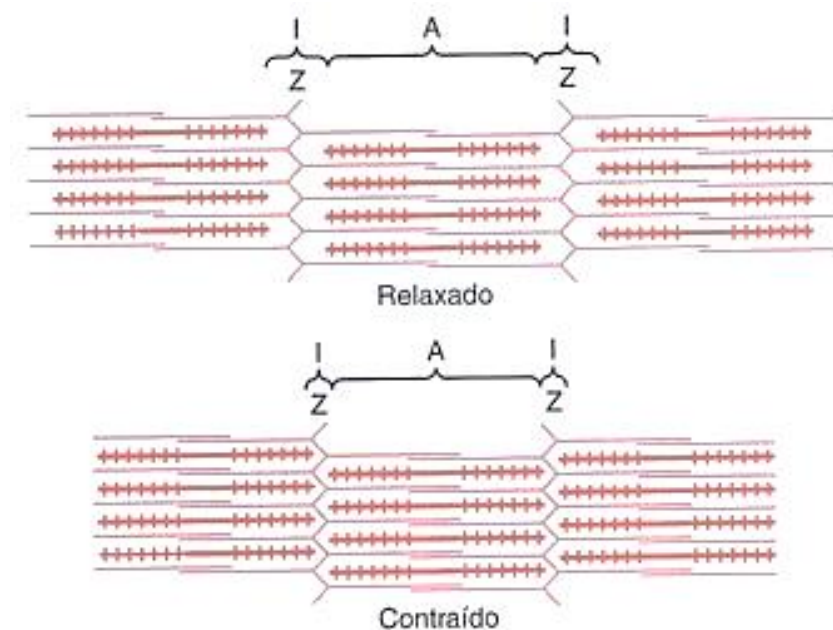


Figura 03: Representação esquemática do sarcômero do músculo estriado esquelético mostrando a disposição dos filamentos grossos e finos no sarcômero e identificando faixas de sobreposição entre eles.

Compreende-se que as fibras musculares possuem um diâmetro consistente independentemente do tamanho do músculo. Além disso, o tamanho da fibra muscular está diretamente relacionado à sua capacidade de gerar força. No entanto, a organização arquitetônica das miofibras em relação ao eixo gerador de força demonstra a versatilidade funcional dos músculos.¹⁸.

Três classes principais de arquitetura muscular foram identificadas ¹⁹ (a) longitudinal, onde as miofibras correm ao longo do comprimento do eixo gerador de força muscular (por exemplo, bíceps); (b) unipennado em que as miofibras correm ao longo de um ângulo fixo do eixo (por exemplo, músculo vasto lateral); e (c) arquitetura multipennada no qual as fibras musculares correm em vários ângulos em relação ao eixo gerador de força do músculo (por exemplo, músculo glúteo médio).

Em nível molecular, a contração sarcomérica é um movimento das cabeças de miosina nos filamentos de actina – chamada ponte cruzada. O ciclo de pontes cruzadas é uma sequência de reações enzimáticas responsáveis pelo movimento das cabeças da miosina nos filamentos de actina, gerando força dentro de cada miofibrila individual, que é experimentada coletivamente pelo músculo. Resumidamente, a geração de força ocorre em seis etapas ²⁰. No início da contração, o Ca^{2+} livre no citosol provoca uma mudança conformacional na troponina, revelando locais de ligação à miosina nos filamentos de actina. A cabeça da miosina balança para fora em direção ao filamento fino em um ângulo de 45° e está em um estado de rigor (rígido). O ATP disponível liga-se à miosina, dissociando brevemente a miosina da actina. A atividade ATPase da miosina hidrolisa ATP em ADP e P_i (fosfato livre) (ainda ligado à miosina) causando o filamento de miosina religa-se fracamente à actina no ângulo de 90° (ponte cruzada) em relação ao filamento de actina. O lançamento de P_i inicia o golpe de força. A cabeça da miosina gira sobre sua dobradiça, empurrando o filamento de actina por ela, em direção à banda M. No final do golpe de força, a cabeça da miosina libera ADP e recupera seu estado de rigor.

1.3- TROFISMO: ATROFIA E HIPERTROFIA MUSCULAR

O trofismo muscular é a capacidade de um músculo para hipertrofiar (aumentar de tamanho) ou atrofiar (diminuir de tamanho). A hipertrofia muscular é o aumento do tamanho das fibras musculares, enquanto a atrofia muscular é a diminuição do tamanho das fibras musculares ²¹. O trofismo muscular é estudado para avaliar a

nutrição e a manutenção da saúde dos músculos, que está diretamente ligada à irrigação de sangue até o músculo e à prática de exercícios físicos ²¹.

O musculo esquelético é plástico, em parte, há um equilíbrio entre a síntese proteica e a degradação proteica. A exposição do musculo esquelético ao estímulo do treinamento físico gera adaptações, como força e hipertrofia (síntese proteica), ao ponto que a inatividade gera à atrofia muscular (degradação proteica). ²²

Hipertrofia muscular é definida como o aumento da massa muscular total. Toda hipertrofia muscular resulta no aumento do número de filamentos de actina e miosina em cada fibra muscular. ¹⁶

Os músculos do corpo são continuamente remodelados para se ajustar às funções que são exigidas deles. Seus diâmetros podem ser alterados, comprimentos, forças, e até mesmo suas fibras musculares, mesmo que discretamente podem ser alteradas. ¹⁶

A ação estressora à célula e à matriz extracelular tem como resultado final a lesão tecidual e orgânica, o que determina o seu padrão morfológico. Uma célula normal está limitada em sua composição e função com uma faixa de variação relativamente estreita por causa do seu estado metabólico, diferenciação e especialização, restrições as células vizinhas, e disponibilidade de substratos metabólicos, conseguindo manter a demanda fisiológica, mantendo assim a homeostase muscular. As adaptações são respostas reversíveis às suas alterações fisiológicas como tamanho, número, fenótipo, atividade metabólica, função das células e resposta ao meio ambiente em que se encontra. ²³

A hipertrofia é o aumento da célula, resultando no aumento do tamanho do órgão afetado. Na ausência de estímulo, a célula tende a retornar ao seu estado original sem sofrer danos. Se ocorrer uma lesão celular, o processo pode ser reversível até certo ponto, mas se o estímulo danoso for persistente e intenso induzindo a alterações funcionais significativas, a lesão se torna irreversível levando a morte celular. Outro agente que pode influenciar na morfologia e na função é o processo de envelhecimento. As causas hipertróficas podem ser fisiológicas ou patológicas devido ao aumento da demanda funcional ou por estimulação de hormônios e fatores de crescimento e o aumento da carga de trabalho muscular é o agente mais comum para a hipertrofia. Uma sequência de fácil entendimento é partindo do miócito normal, a ação estressora evoluindo para a adaptação ao aumento de carga resultando em miócito adaptado (hipertrofia) ²³.

A hipertrofia muscular é um processo adaptativo que ocorre em resposta ao treinamento de força e é um dos principais mecanismos responsáveis pelo aumento da força muscular ²⁴. A hipertrofia muscular é influenciada por vários fatores, como a intensidade do treinamento, o volume do treinamento, a frequência do treinamento, a duração do treinamento e a nutrição adequada.

A atrofia muscular pode ser causada por várias condições, como a falta de uso muscular, a imobilização, a desnutrição, a doença e o envelhecimento. A atrofia muscular pode levar à perda de força muscular e à diminuição da capacidade funcional ²⁴.

2- REVISÃO DE LITERATURA

2.1- Medidas De Ultrassom E Grau De Confiabilidade

Desde os seus primeiros relatos na literatura, imagens de cortes anatômicos vêm sendo utilizados com a finalidade de avaliar o tecido muscular com um alto grau de precisão e confiabilidade através de procedimentos tal como a ressonância magnética (RM), que permite uma avaliação precisa sobre o tecido muscular, desde análise de áreas de secção transversa (AST)²⁴, ou com a finalidade de diagnosticar lesões musculares²⁵.

Porém seu uso se limita a ambientes laboratoriais tornando-se um procedimento o tanto quanto inviável para medição em ambientes clínicos, além de seu alto custo. Portanto se fez necessário o uso de novas técnicas e ferramentas com a finalidade de identificar imagens de áreas musculares que apresentem um alto grau de validade e acessíveis. Uma ferramenta que vem sendo explorada dentro de ambientes clínicos é o aparelho de ultrassonografia modo-B que é capaz de gerar imagens de grupamentos musculares com Coeficientes de generalização (G) para medidas de espessura muscular superiores a 0,92 indicando que o ultrassom em modo B é um método altamente confiável para a medição das espessuras de músculo em homens e mulheres²⁶ sugerindo que as medições de ultrassom podem ser aplicadas em avaliações clínicas, após a validação dos procedimentos lacunas foram deixadas sobre sua aplicabilidade em relação ao protocolo de rm, partindo desse pressuposto um grupo de pesquisa comparou avaliações de imagens de ultrassom e de ressonância magnética a fim de averiguar sua viabilidade e o quão preciso ou não seria essas medidas, em suas conclusões finais foi exposto uma relação positiva para imagens de rm e ultrassom é sobre a ótica de espessura muscular tanto para membros inferiores com membros superiores²⁷, neste contexto a utilização do ultrassom, devido a sua popularidade seu fácil manuseio e coeficientes de correlação intraexaminadores variando de 0,90 a 0,99²⁸ mostrando sua efetividade, compondo inúmeras metodologias de artigos acadêmicos que se propõe a avaliar mudanças a nível de estrutura muscular²⁹.

Dessa forma antes de iniciar qualquer tipo de procedimento de análise de ultrassonografia tem-se que executar um protocolo cujo objetivo avalie as medidas intra-avaliador e entre avaliadores elegendo assim um grau de confiabilidade para as medidas realizadas evitando qualquer potencial de viés. Por isso a necessidade de

se fazer uma pesquisa para validar e comprovar que realmente é uma técnica confiável.

3- Objetivos

3.1- Objetivo geral

Determinar a validade de medidas de ultrassonografia para área de secção transversa muscular.

3.2- Objetivos Específicos

- Determinar a confiabilidade da medida de espessura muscular (EM) do reto femoral intra avaliador, inter avaliadores, bem como, inter dias;
- Apresentar o erro típico da medida (ETM) absoluto e relativo para as medidas de EM nas condições intra avaliador, inter avaliadores, bem como, inter dias;
- Estratificar a espessura muscular do reto femoral (EM) de uma determinada população em percentis;
- Comparar as médias da EM entre sexos (geral) e considerando um conjunto de dados estratificados por percentil menor que 50% e maior que 50%;
- Analisar se a idade poderia ser um bom preditor para alterações na EM.

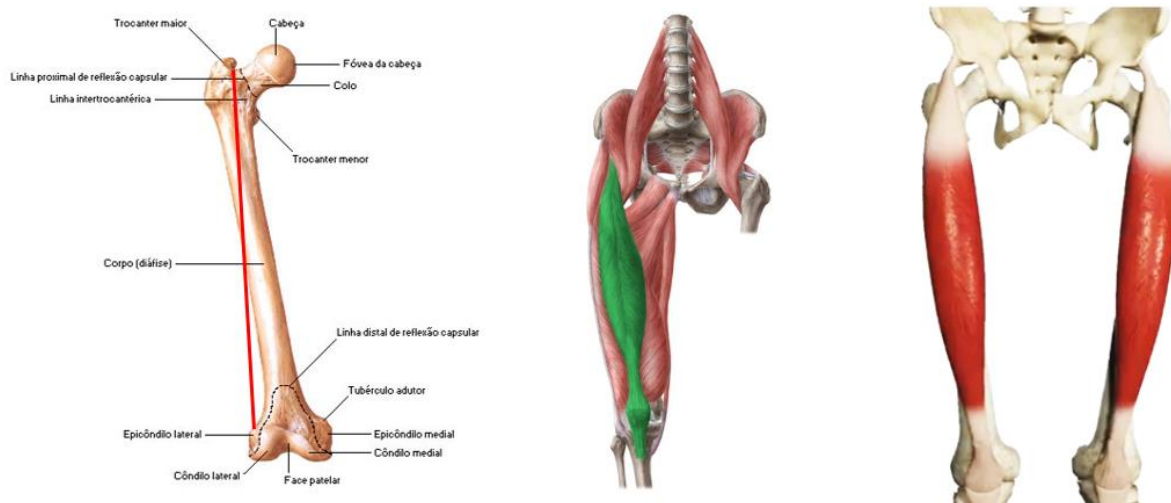
4- MATERIAIS E MÉTODOS

A ultrassonografia Mindray modelo M6 foi usada para determinar a espessura do reto femoral (RF) usando um transdutor linear com frequência de 6-14 megahertz (MHz) modelo L14-6Ns. Foram adotados os pontos anatômicos do trocânter maior e epicôndilo lateral do fêmur da coxa direita, em seguida o posicionamento de 40% do comprimento do fêmur para a região proximal para a análise de espessura do músculo reto femoral (RF).

Medidas para realização da ultrassom



Figura 04: Padronização das medidas para realização do ultrassom.



Antes de iniciar o experimento, procedeu-se à realização de marcações metículosas sobre a pele, utilizando uma caneta, com o propósito de estabelecer uma padronização nas distâncias entre os pontos anatômicos que serviram como referência para o posicionamento do transdutor. Todas as medidas foram executadas no

membro direito dos participantes. Para a captura das imagens, os indivíduos assumiram a posição de decúbito dorsal sobre uma maca, mantendo as pernas completamente estendidas e os músculos relaxados por um período cronometrado de 10 minutos.

Durante esse procedimento, uma quantidade substancial de gel para ultrassom, solúvel em água de contato, foi aplicado de maneira generosa. Essa aplicação ocorreu diretamente sobre o transdutor, visando minimizar a distorção das imagens e facilitar o acoplamento acústico necessário para a realização do estudo.

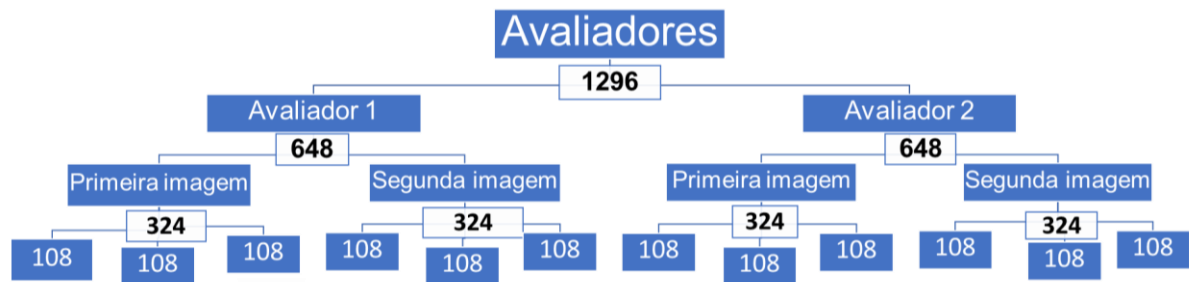


Figura 05: Total de medidas realizadas. Fonte: Autor

Todas as visitas foram realizadas no mesmo período e local climatizado o qual contou com a presença de um profissional treinado a fim de assegurar a validade dos procedimentos acima listados.



Figura 06: Aparelho de ultrassonografia Mindray modelo M6

O estudo foi aprovado pelo Comitê de Ética em Pesquisa em Seres Humanos do Universidade Evangélica de Goiás (UniEvangélica), conforme parecer CEP nº 6.210.982, com o Certificado de Apresentação para Apreciação Ética (CAAE) nº 69796523.7.0000.5076 e os que indivíduos concordaram em participar e assinaram um Termo de Consentimento Livre e Esclarecido (TCLE), conforme resolução 196/96 do Conselho Nacional de Saúde (CNS).

4.1- DELINEAMENTO DO ESTUDO

Estudo contou com Cento e Oito (108) participantes de ambos os sexos, com idade entre 18 e 67 anos.

O Projeto foi composto por 03 fases, conforme podemos observar no esquema abaixo (figura 07).

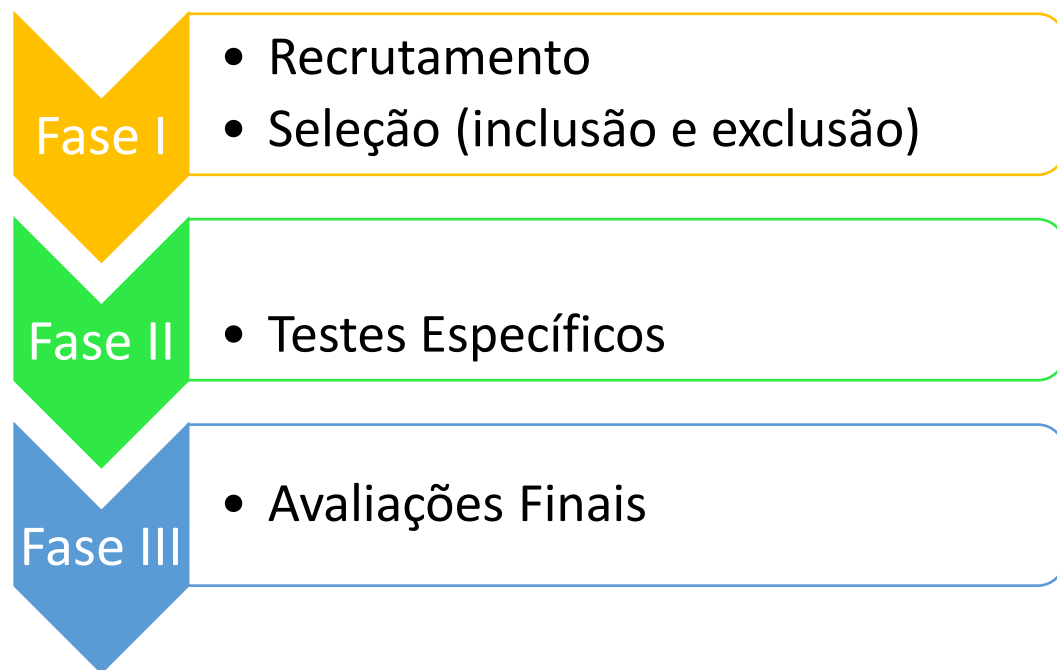


Figura 07: Diagrama das Fases do Estudo

O Recrutamento e seleção foi iniciado em agosto de 2023, imediatamente após a aprovação do Protocolo pelo Comitê de Ética em Pesquisa com Seres Humanos da Universidade Evangélica de Goiás.

Os participantes de pesquisa foram recrutados na comunidade da cidade de Anápolis - Goiás. Os participantes que se enquadraram nos critérios de inclusão/exclusão foram convidados a participar do estudo. Os que, após um esclarecimento inicial sobre as condições da pesquisa clínica, em princípio concordaram, foram encaminhados para realização de consulta e avaliações iniciais, ocasião em que receberam novamente as explicações sobre todos os detalhes referentes ao estudo e todos os demais aspectos mencionados no TCLE e assim o assinaram.

Duração Esperada da Participação dos Participantes de Pesquisa e Descrição da Sequência e Duração das Etapas, Incluindo Follow-Up

4.2- CRITÉRIOS DE INCLUSÃO

Os seguintes critérios devem ser satisfeitos para que o participante de pesquisa fosse incluído no estudo:

- Participantes de pesquisa de ambos os sexos (masculino e feminino) com idade entre 18 e 67 anos.
- Sem outras doenças significativas, que possam impactar sua participação no estudo, de acordo com as regras definidas no Protocolo, e avaliações a que foi sub-

metido: história clínica, medidas de pressão e pulso, exame físico e exames complementares;

- Capaz de compreender a natureza e objetivo do estudo, com intenção de cooperar com o pesquisador e agir de acordo com os requerimentos de todo o ensaio, o que vem a ser confirmado mediante a assinatura do Termo de Consentimento Livre e Esclarecido.

4.3- CRITÉRIOS DE EXCLUSÃO

A resposta positiva a qualquer um dos seguintes critérios excluirá o participante de pesquisa do estudo:

- Participante com evidência atual de doenças clinicamente significativas, que impeça a participação do indivíduo no estudo;
- Efetou qualquer tratamento prévio que, a juízo do pesquisador principal, possa interferir nos objetivos do estudo;
 - O paciente tenha alguma doença osteomuscular.

4.4- AVALIAÇÃO CLÍNICA/ FÍSICA GERAL

Avaliação clínica: foi realizada a história clínica com entrevista aos pacientes.

Sinais Vitais e Antropometria: pressão arterial sistólica e diastólica na posição sentada, batimento cardíaco (pulso), temperatura axilar em °C, medições de peso e estatura, e índice de massa corporal (IMC).

Orientações: a estatura e o peso deverão ser medidas apenas na primeira visita.

A pressão arterial foi considerada como normal dentro dos seguintes limites: 90-139 mmHg para a sistólica e 50-89 mmHg para a diastólica. O pulso dentro de 50-100 bpm será considerado normal.

4.5- Cálculo amostral

A amostra para o estudo de reprodutibilidade foi estabelecida considerando os testes a serem realizados (correlação interclasse), poder de 80%, tamanho de efeito médio de 0,5, nível e significância 5% sendo necessários 52 participantes.³⁰

Para a análise de repetibilidade foi usado o software G*Power (versão 3.0), considerada a coleta com dois grupos e três medidas do mesmo participante (ANOVA para medidas repetidas) para cada grupo, poder de 95%, tamanho de efeito médio (f) de 0,25, nível e significância 5% e perdas de 20% sendo necessários 86 participantes.

4.6- Análise estatística

A construção da análise foi baseada nos conceitos de reprodutibilidade da técnica (inter e intra observadores ou avaliadores) e repetibilidade das medidas, que também podem ser intra e inter-observadores. Se for utilizar dois avaliadores e cada um deles fizer pelo menos três medidas.

Os resultados foram descritos como média e desvio-padrão para variáveis com distribuição normal (Gaussiana) e mediana e intervalo de confiança de 95% ((IC 95%) para distribuição não-normal. O teste usado para verificar a distribuição foi o teste de Shapiro-Wilk (<50 observações) ou teste de Kolmogorov-Smirnov (> 50 observações). A análise foi conduzida usando uma medida e/ou a médias das três medidas.

4.6.1- Reprodutibilidade

Reprodutibilidade: inclui se a técnica ou o instrumento a ser utilizado segue o mesmo padrão, sem gerar erros. Quando a técnica ou o instrumento pode ser replicado com alto grau de confiabilidade³¹.

A concordância entre as medidas (boa ou ruim) foram detectadas por dois avaliadores experiente. O teste utilizado será o coeficiente kappa com a seguinte classificação:

- Kappa <0 – nenhuma concordância;
- 0 - 0,20 – pobre concordância;
- > 0,20 – 0,40 – concordância fraca;
- > 0,40 – 0,60 – concordância moderada
- > 0,60 - 0.80 – concordância substancial
- > 0,80 - 1.00 - concordância perfeita

O coeficiente de correlação intraclass (ICC) foi usado para verificar a concordância entre as medidas contínuas. Sendo assim realizado com as medias unicas e com as médias das medidas. A classificação da correlação foi a seguinte:

- 0: ausência;

- 0–0,19: ruim;
- 0,20–0,39: fraca;
- 0,40–0,59: moderada;
- 0,60–0,79: substancial;
- 0,80: alta

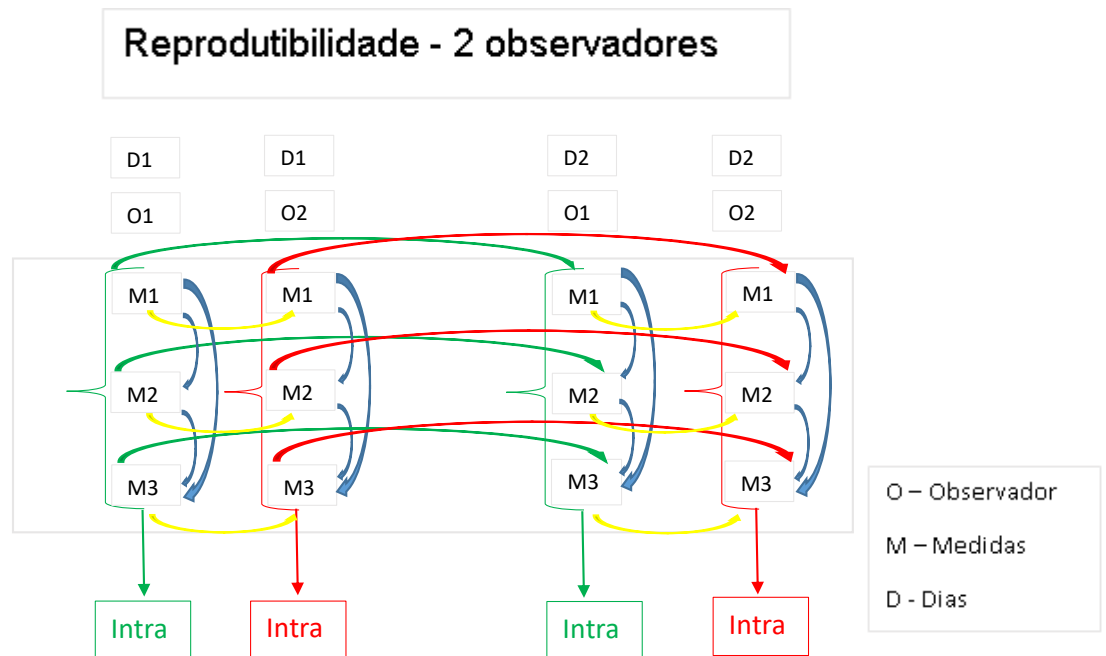


Figura 08: Diagrama dos Grupos experimentais do estudo para reprodutibilidade.

4.6.2- Repetibilidade

Repetibilidade ou teste-reteste de repetibilidade: vai descrever a variação de sucessivas medidas realizadas da mesma variável sob as mesmas condições³².

A análise de variância (ANOVA) para medidas repetidas com *post hoc* de Bonferroni (aqui estreitar o valor de p de acordo com o número de medidas coletadas para reduzir erro tipo I. Se no caso for 3, $p = 0,05/3$ ou seja, 0,017).

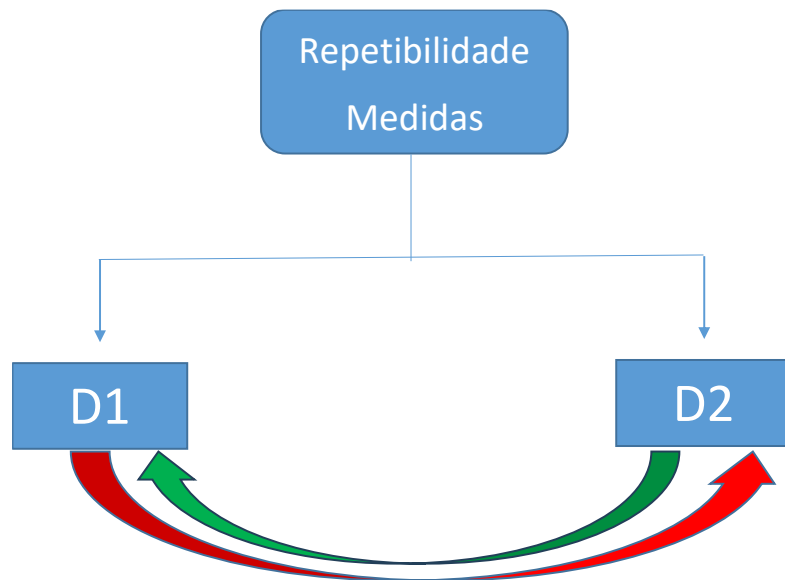


Figura 09: Diagrama dos Grupos experimentais do estudo para repetibilidade

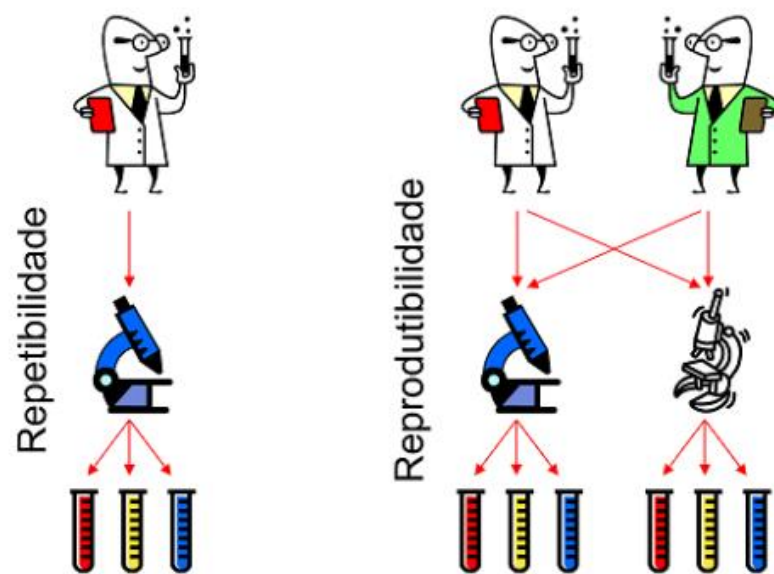


Figura 10: Diferença entre repetibilidade e reprodutibilidade Fonte: (33)

5- Resultados

Após análise dos pressupostos estatísticos, os dados foram descritos por média e desvio padrão e intervalo de confiança para 95%. A característica da amostra utilizada é descrita na Tabela 1. A análise de normalidade por Shapiro-Wilk demonstrou distribuição normal para os dados de medidas repetidas da EM do reto femoral ($p = 0,815$; $p = 0,175$), tanto para homens, quanto para mulheres.

Tabela 1. Características da amostra (N = 108)

	Masculino (N = 50)				Feminino (N = 58)			
	Idade (anos)	IC 95% (inf-sup)	EM (cm)	IC 95% (inf-sup)	Idade (anos)	IC 95% (inf-sup)	EM (cm)	IC 95% (inf-sup)
Média	36,0	31,9 - 40,0	2,41	2,30 - 2,52	29,9	26,2 - 33,5	1,86	1,77 - 1,93
DP	14,1		0,38		14,0		0,31	

Legenda: DP = desvio padrão; EM = espessura muscular

A análise do coeficiente de correlação intraclassa (CCI) intra avaliador (consistência interna da medida) apresentou excelente classificação para o avaliador 1 (Visita 1; CCI = 0,998; $p = 0,0001$ – Visita 2; CCI = 0,998; $p = 0,0001$) e para o avaliador 2 (Visita 1; CCI = 0,997; $p = 0,0001$ – Visita 2; CCI = 0,998; $p = 0,0001$).

Quando analisamos a confiabilidade entre avaliadores numa mesma sessão (sessão 1), observamos uma CCI = 0,994 ($p = 0,0001$). O mesmo ocorreu nas medidas entre avaliadores na sessão 2 (CCI = 0,994; $p = 0,0001$).

Por fim, quando avaliamos a confiabilidade entre as sessões de medidas da EM do reto femoral (estabilidade), foi observado um CCI = 0,963 ($p = 0,0001$) para o avaliador 1 e um CCI = 0,962 ($p = 0,0001$).

A Tabela 2 apresenta o ETM relativo e absoluto para todas as análises de confiabilidade realizadas.

Tabela 2. Apresentação do ETM relativo e absoluto para as medidas de EM observadas para as sessões de avaliação e os diferentes avaliadores.

	Consistência Interna				Inter Avaliadores		Inter Dias	
	Sessão 1		Sessão 2		Sessão 1	Sessão 2	Aval 1	Aval 2
	Aval 1	Aval 2	Aval 1	Aval 2				
ETM Abs (cm)	0,03	0,03	0,03	0,04	0,10	0,09	0,11	0,11
ETM Rel (%)	1,3	1,5	1,3	1,5	4,8	4,7	5,7	5,5

Legenda: ETM= erro típico de medida; Aval = avaliador; Abs = absoluto; Rel = relativo

Além disso, os dados foram estratificados por idade e sexo e separados no momento de entrada para análise no software estatístico, sendo calculado e descrito em forma de percentil. A Tabela 3 apresenta os valores percentis estratificados para a EM do reto femoral.

Tabela 3. Distribuição dos dados experimentais por percentil.

		Percentis						
		5	10	25	50	75	90	95
EM (cm)	Masc	1,58	1,65	2,12	2,45	2,64	2,82	2,92
	Fem	1,39	1,50	1,65	1,83	2,03	2,32	2,38

Legenda: EM = espessura muscular

Conforme esperado, o teste T para amostras independentes apresentou diferenças significativas quando comparado os sexos para a média de EM dos dois avaliadores ($2,41 \pm 0,48$ cm vs. $1,86 \pm 0,31$ cm, respectivamente para homens e mulheres; $p = 0,0001$). Quando comparamos as médias de EM entre os dados estratificados menores que percentil 50% e maiores que percentil 50%, foi observado diferenças significativas ($p < 0,001$ e $p < 0,001$, respectivamente). A tabela 4 apresenta os dados comparativos entre homens e mulheres segundo a estratificação por percentil.

Tabela 4. Comparativo entre a EM do reto femoral entre os sexos masculinos e femininos considerando a estratificação por percentil abaixo e acima da média populacional.

	Masculino		Feminino	
	Percentil <50% (N = 24)	Percentil >50% (N = 26)	Percentil <50% (N = 28)	Percentil >50% (N = 30)
Média (cm)	2,11*	2,68**	1,61*	2,09**
DP	0,26	0,20	0,16	0,20

Legenda: * comparação teste T entre percentil <50% entre homens e mulheres; ** comparação teste T entre percentil >50% entre homens e mulheres.

Após sustentação dos pressupostos de distribuição dos resíduos, homocedasticidade, bem como, a linearidade do comportamento dos dados, a análise de regressão linear demonstrou que a idade para as mulheres é um preditor significativo para a EM, porém fraco ($r = -0,431$; $R^2 = 0,186$; $p = 0,001$), sugerindo que as alterações do volume muscular ao longo do tempo sofrem influência (18%) e podem ser estimadas a partir da idade [$F(1,56) = 12,761$; $p = 0,001$]. Entretanto, a idade não representa uma variável determinante da EM para homens ($r = -0,06$; $R^2 = 0,004$ -

[$F(1,46) = 0,207$; $p = 0,651$]). A equação de estimativa da EM pela idade em mulheres pode ser descrita por: $2,139 - 0,009 \times \text{idade (anos)}$. A Figura 10 apresenta a reta de regressão para EM a partir da idade.

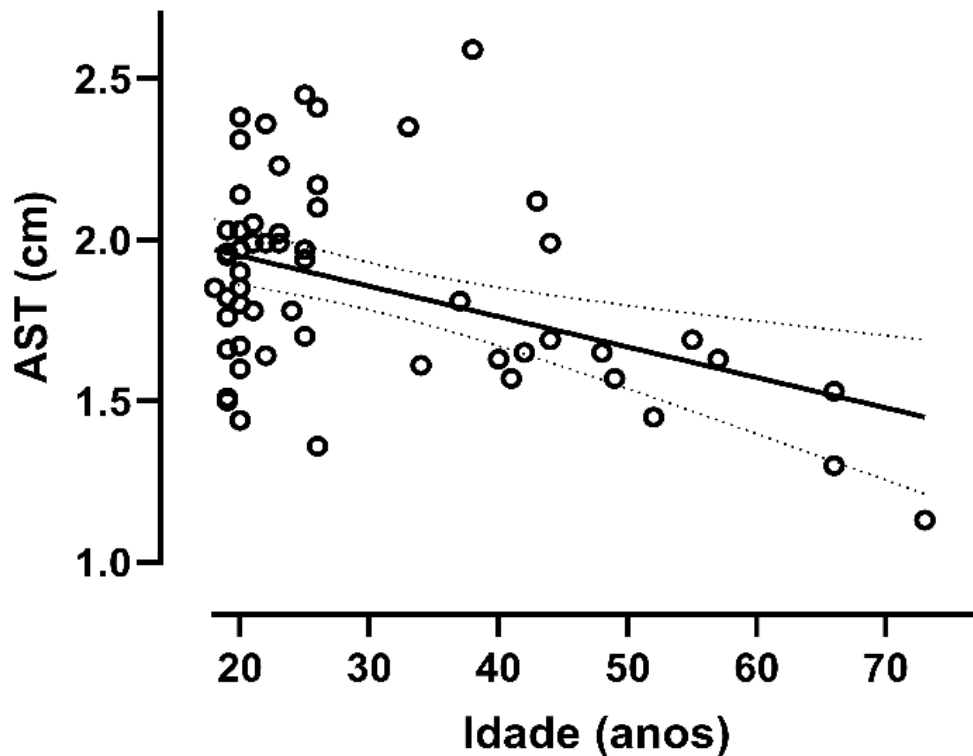


Figura 11. Representação a reta de regressão para predição da EM do reto femoral feminina a partir da idade.

A variabilidade inter avaliadores observada pode ser atribuída a nuances na técnica de aquisição de imagens e interpretações subjetivas durante a análise. Essa descoberta ressalta a importância de protocolos padronizados e treinamento contínuo para garantir resultados uniformes entre diferentes profissionais. No entanto, a estabilidade temporal das medidas fortalece a validade da ultrassonografia modo-B em estudos longitudinais e intervenções terapêuticas.

A análise da reprodutibilidade das medidas de área de seção transversa do músculo reto femoral por meio da ultrassonografia revela resultados que têm implicações significativas para a prática clínica e pesquisa em ciências do movimento. A consistência intra avaliador foi notável, indicando que um mesmo examinador, ao repetir as medições, obteve resultados bastante semelhantes. Essa consistência é um indicativo positivo da confiabilidade da técnica, sugerindo que ela pode ser utilizada de forma consistente por um mesmo profissional.

Entretanto, ao explorar a reprodutibilidade inter avaliadores, observou-se uma variabilidade que, embora esperada em certa medida, merece atenção. Diferenças significativas entre avaliadores podem surgir por uma variedade de razões, desde variações na técnica de aquisição de imagens até interpretações subjetivas durante a análise das mesmas. Estratégias para minimizar essas discrepâncias, como treinamento padronizado dos avaliadores, podem ser implementadas para melhorar a consistência entre diferentes profissionais.

Outro ponto relevante é a estabilidade das medidas ao longo do tempo. Os resultados indicaram uma boa confiabilidade temporal, sugerindo que as medições de área de secção transversa muscular obtidas por ultrassonografia mantiveram-se consistentes em diferentes dias. Essa estabilidade é crucial para estudos longitudinais e intervenções terapêuticas, proporcionando uma base sólida para avaliar mudanças na composição corporal ao longo do tempo.

6- Discussão

A confiabilidade estatística entre duas medidas clínicas é uma medida da consistência entre as duas medidas. Ela é definida como a proporção da variância total que é atribuível à variação real entre os indivíduos, em oposição à variação devido a erros de medição ³⁴. A confiabilidade pode ser avaliada por meio de várias estatísticas, como o coeficiente de correlação intraclass (ICC) e o coeficiente de concordância de Kappa ³⁵. O ICC é uma medida de confiabilidade que avalia a consistência entre as medidas contínuas, enquanto o coeficiente de concordância de Kappa é usado para avaliar a confiabilidade entre as medidas categóricas ³⁵.

A confiabilidade é uma medida importante na avaliação de medidas clínicas, pois indica a precisão e consistência das medidas. Uma medida com alta confiabilidade é considerada mais precisa e consistente do que uma medida com baixa confiabilidade ³⁴. A confiabilidade também é importante na avaliação da validade de uma medida, pois uma medida não pode ser válida se não for confiável ³⁴.

A reprodutibilidade estatística entre duas medidas clínicas é uma medida da consistência entre as duas medidas. Ela é definida como a capacidade de um método de medição produzir resultados consistentes quando aplicado repetidamente em uma mesma amostra ³⁵. A reprodutibilidade pode ser avaliada por meio de várias estatísticas, como o coeficiente de correlação intraclass (ICC) e o coeficiente de concordância de Kappa ³⁵. O ICC é uma medida de reprodutibilidade que avalia a consistência entre as medidas contínuas, enquanto o coeficiente de concordância de Kappa é usado para avaliar a reprodutibilidade entre as medidas categóricas ³⁵.

A reprodutibilidade é uma medida importante na avaliação de medidas clínicas, pois indica a precisão e consistência das medidas. Uma medida com alta reprodutibilidade é considerada mais precisa e consistente do que uma medida com baixa reprodutibilidade ³⁴. A reprodutibilidade também é importante na avaliação da validade de uma medida, pois uma medida não pode ser válida se não for reprodutível ³⁶.

A confiabilidade intraavaliador foi avaliada através da comparação das medidas de área de secção transversa do reto femoral realizadas pelo mesmo avaliador em diferentes momentos. Os resultados indicam uma consistência notável nas medições intraavaliadoras, sugerindo uma alta confiabilidade na repetição das análises por um único avaliador ao longo do tempo.

A confiabilidade interavaliador foi avaliada pela comparação das medidas de área de secção transversa do reto femoral entre diferentes avaliadores. Os resulta-

dos revelam uma concordância satisfatória entre os avaliadores, indicando que as medições são consistentes independentemente do observador. Esse aspecto é crucial para assegurar a robustez e a validade das medidas obtidas.

É importante ressaltar que a confiabilidade intra e interavaliadores é essencial na obtenção de dados precisos e na garantia da consistência das medições ao longo do tempo e entre diferentes avaliadores. A confiabilidade apresentada fortalece a credibilidade dos resultados obtidos, fornecendo uma base sólida para a interpretação e aplicação dos dados nas investigações relacionadas à área de secção transversa do reto femoral.

A observação de variações nas medidas ao longo de diferentes dias em estudos de confiabilidade intraavaliador levanta questões significativas sobre a consistência das medições ao longo do tempo. Considerando análises estatísticas e interpretações potenciais: o teste de repetibilidade forneceu uma medida quantitativa da consistência intraavaliador ao longo do tempo. Com os testes de Bland-Altman foi possível visualizar a concordância entre as medidas em diferentes dias.

A avaliação da validade interna e externa de um estudo é crucial para compreender a solidez e a aplicabilidade dos resultados. Analisamos esses aspectos em relação ao estudo sobre a confiabilidade intra e interavaliadores nas medidas da área de secção transversa do reto femoral: O controle de variáveis, como a condição física dos participantes, contribuiu para a validade interna. E a seleção de uma amostra diversificada e representativa da população alvo contribui para a validade interna.

As medidas da área de secção transversa do reto femoral podem ser incorporadas em protocolos clínicos para avaliação da condição muscular em pacientes com diversas condições de saúde.

Futuros estudos podem explorar a confiabilidade das medidas em programas de pesquisa de longo prazo, fornecendo insights sobre a estabilidade das características musculares ao longo do tempo.

A avaliação contínua da condição muscular pode influenciar protocolos de treinamento. Profissionais de saúde podem utilizar essas medidas para adaptar programas de exercícios, monitorar a eficácia do treinamento e personalizar intervenções de reabilitação.

Essas implicações práticas destacam a relevância dos resultados deste estudo na otimização da prática clínica e na orientação de pesquisas futuras. A compreensão das nuances da confiabilidade nas medidas da área de secção transversa do

reto femoral é crucial para a aplicação eficaz dessas técnicas em ambientes clínicos e de pesquisa.

Profissionais de reabilitação ou fisioterapeutas podem usar essas medidas para monitorar como os pacientes respondem a tratamentos específicos, ajustando as intervenções conforme necessário.

Profissionais de saúde podem utilizar essas medidas para adaptar programas de treinamento, otimizando a prescrição de exercícios com base na análise específica da área de secção transversa do reto femoral.

Em contextos esportivos, por exemplo, a análise da área de secção transversa do reto femoral pode ser incorporada para avaliar a eficácia de programas de treinamento na prevenção de lesões e no aprimoramento do desempenho atlético.

Os resultados deste estudo têm relevância clínica substancial, oferecendo insights importantes para profissionais de saúde envolvidos em diagnóstico, monitoramento e intervenções relacionadas à área de secção transversa do reto femoral. A compreensão da confiabilidade dessas medidas é essencial para garantir uma abordagem clínica precisa e eficaz em diversas condições e contextos.

A presente pesquisa fez uma contribuição valiosa ao conhecimento existente na área da avaliação da área de secção transversa do reto femoral, destacando-se por fornecer insights específicos sobre a confiabilidade intra e interavaliadores dessa medida.

Em contraste com nossos achados, Hammond et al.¹² e Takahashi et al.¹³ descobriram que a confiabilidade relativa entre avaliadores do procedimento em indivíduos saudáveis era apenas aceitável. Da mesma forma, Lima et al.¹⁶ relataram que a confiabilidade relativa entre dias é apenas aceitável. As discrepâncias podem ser resultado do menor tamanho amostral nos três estudos (106 versus 12-15 indivíduos saudáveis), ou seja, erro aleatório. A variação na experiência do avaliador é outra explicação plausível¹². Nossos valores de ICC entre avaliadores também são mais elevados do que em estudos sobre o tema que incluíram pacientes^{12, 15, 17}.

Em resumo, esta pesquisa não apenas confirma e valida aspectos previamente estabelecidos na literatura, mas também expande o conhecimento existente ao explorar novas dimensões, como variáveis ambientais, técnicas de medição detalhadas e adaptações para diferentes populações. Ao oferecer uma análise mais abrangente e específica, esta pesquisa adiciona nuances valiosas à compreensão da confiabilidade das medidas da área de secção transversa do reto femoral, contribuindo de maneira significativa para o avanço da área.

7- Conclusões

Os resultados mostraram a confiabilidade intra e entre avaliadores com ICC 0,9 e $P < 0,001$. Portanto, o ultrassom modo-B é uma ferramenta confiável para medição de espessura muscular. Essa análise ajudou a estabelecer a validade e a consistência dos métodos de medição utilizados, permitindo que os pesquisadores e profissionais da saúde façam inferências precisas e tomem decisões informadas com base nesses resultados.

A consistência intraavaliador sugere sua aplicabilidade por um mesmo profissional em diferentes momentos. A variabilidade interavaliadores ressalta a necessidade de abordagens padronizadas. A estabilidade temporal das medidas reforça sua utilidade em estudos de acompanhamento.

Em última análise, este estudo contribui para o avanço do conhecimento na área, fornecendo evidências sólidas sobre a confiabilidade da ultrassonografia modo-B na avaliação da musculatura, abrindo portas para aplicações clínicas e científicas mais robustas e confiáveis.

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9- Anexos

9.1 Anexo 1 – Termo de consentimento livre e esclarecido

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (TCLE)

ANÁLISE DE REPRODUTIBILIDADE E REPETIBILIDADE EM MEDIDAS DE ÁREA DE SECÇÃO TRANSVERSAL MUSCULAR COM ULTRASSONOGRAFIA: UM ESTUDO DE AVALIAÇÃO INTERDIAS E INTRA/INTER AVALIADORES.

Prezado participante,

Você está sendo convidado(a) para participar da pesquisa (ANÁLISE DE REPRODUTIBILIDADE E REPETIBILIDADE EM MEDIDAS DE ÁREA DE SECÇÃO TRANSVERSAL MUSCULAR COM ULTRASSONOGRAFIA: UM ESTUDO DE AVALIAÇÃO INTERDIAS E INTRA/INTER AVALIADORES).

Desenvolvida por Katielle Rodrigues da Silva Cardoso, discente de mestrado em Movimento Humano e Reabilitação da Universidade Evangélica de Goiás - UniE-VANGÉLICA, sob orientação do Professor(a) Dr. Rodrigo Álvaro Brandão Lopes Martins.”

O objetivo central do estudo é: Determinar a validade de medidas de ultrassonografia modo-B, intra e entre avaliadores, com um coeficiente de correlação sobre a espessura muscular do reto femoral.

O convite a sua participação se deve à atender todos os critérios de inclusão para a pesquisa:

- Participantes de pesquisa de ambos os sexos (masculino e feminino) com idade entre 18 e 67 anos.
- Capacidade cognitiva preservada
- Sem outras doenças significativas, que possam impactar sua participação no estudo, de acordo com as regras definidas no Protocolo, e avaliações a que foi submetido: história clínica, medidas de pressão e pulso e exame físico.
- Capaz de compreender a natureza e objetivo do estudo, com intenção de cooperar com o pesquisador e agir de acordo com os requerimentos de todo o ensaio, o que vem a ser confirmado mediante a assinatura do Termo de Consentimento Livre e Esclarecido.

Sua participação é voluntária, isto é, ela não é obrigatória e você tem plena autonomia para decidir se quer ou não participar, bem como retirar sua participação a qualquer momento. Você não será penalizado de nenhuma maneira caso decida não consentir sua participação, ou desistir da mesma. Contudo, ela é muito importante para a execução da pesquisa.”

“Serão garantidas a confidencialidade e a privacidade das informações por você prestadas.”

“Qualquer dado que possa identificá-lo será omitido na divulgação dos resultados da pesquisa e o material armazenado em local seguro.”

“A qualquer momento, durante a pesquisa, ou posteriormente, você poderá solicitar do pesquisador informações sobre sua participação e/ou sobre a pesquisa, o que poderá ser feito através dos meios de contato explicitados neste Termo.

A sua participação consistirá em se deitar em uma maca na posição de decúbito dorsal mantendo as pernas completamente estendidas e os músculos relaxados por um período cronometrado de 10 minutos.

Antes de iniciar o experimento, será realizada as marcações meticulosas sobre a pele, utilizando uma caneta, com o propósito de estabelecer uma padronização nas distâncias entre os pontos anatômicos que servirão como referência para o posicionamento da sonda. Todas as medidas serão executadas no membro direito dos participantes.

Durante esse procedimento, uma quantidade substancial de gel para ultrassom, solúvel em água de contato, será aplicado de maneira generosa. Essa aplicação ocorrerá diretamente sobre o transdutor, visando minimizar a distorção das imagens e facilitar o acoplamento acústico necessário para a realização do estudo.

O tempo de duração da coleta é de aproximadamente vinte minutos.

“Ao final da pesquisa, todo material será mantido em arquivo, por pelo menos 5 anos, conforme Resolução 466/12 e orientações do CEP/UniEVANGÉLICA”.

Os resultados serão divulgados em palestras dirigidas ao público participante, relatórios individuais para os entrevistados, artigos científicos e na dissertação/tese.

Assinatura do Pesquisador Responsável – (Inserção na) UniEVANGÉLICA

Contato com o(a) pesquisador(a) responsável: Nome e telefone (a cobrar)

Endereço: Avenida Universitária, Km 3,5 Cidade Universitária – Anápolis/GO CEP: 75083-580

CONSENTIMENTO DA PARTICIPAÇÃO DA PESSOA COMO PARTICIPANTE DE PESQUISA

Eu, _____ CPF nº _____, abaixo assinado, concordo voluntariamente em participar do estudo acima descrito, como participante. Declaro ter sido devidamente informado e esclarecido pelo pesquisador _____ sobre os objetivos da pesquisa, os procedimentos nela envolvidos, assim como os possíveis riscos e benefícios envolvidos na minha participação. Foi-me dada a oportunidade de fazer perguntas e recebi telefones para entrar em contato, a cobrar, caso tenha dúvidas. Fui orientado para entrar em contato com o CEP - UniEVANGÉLICA (telefone 3310-6736), caso me sinta lesado ou prejudicado. Foi-me garantido que não sou obrigado a participar da pesquisa e posso desistir a qualquer momento, sem qualquer penalidade. Recebi uma via deste documento.

Anápolis, ____ de _____ de 20 ____.

Assinatura do participante da pesquisa

Testemunhas (não ligadas à equipe de pesquisadores):

Nome: _____ Assinatura: _____

Nome: _____ Assinatura: _____

Em caso de dúvida quanto à condução ética do estudo, entre em contato com o Comitê de Ética em Pesquisa da UniEVANGÉLICA:

Tel e Fax - (0XX) 62- 33106736

E-mail: cep@unievangelica.edu.br

9.2 Anexo 2- Reliability of real-time ultrasonography assessment of the rectus femoris muscle cross-sectional area: intra-rater, inter-rater, and inter-day analysis

Reliability of real-time ultrasonography assessment of the rectus femoris muscle cross-sectional area: intra-rater, inter-rater, and inter-day analysis

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Abstract

Background The rectus femoris muscle plays an important role in maintaining lower limb stability and biomechanical control during basic physical activities. Both reduced quadriceps strength and decreased muscle thickness (cross-sectional area) of the rectus femoris measured by real-time ultrasonography (RTU) are associated with an increased risk of falls in older adults. We estimated the relative and absolute intra-rater, inter-rater, and inter-day reliability of the procedure.

Methods A 36-year-old female biologist with a master's degree in human movement and rehabilitation and a 28-year-old male physical educator with a master's degree in human movement and rehabilitation measured the cross-sectional area of the right-sided rectus femoris muscle with RTU in 106 healthy persons (58 females and 48 males) aged between 18 and 73. The raters were experienced with the procedure. Each rater conducted three measurements per subject during each visit, with two visits scheduled 7-10 days apart. We estimated the Intraclass Correlation Coefficients (ICC) two-way mixed and 95% minimal detectable difference (MDD).

Results The mean muscle thickness was 2.12 cm. The reliability based on single measurements was as follows: The intra-rater ICC for raters A and B was 0.998 at both visits (MDDs = 0.074-0.082 cm). The inter-rater ICC was 0.976 at visit 1 and 0.977 at visit 2 (MDDs = 0.269-0.270 cm). The inter-day ICC was 0.973 for rater A and 0.972 for rater B (MDDs = 0.286-0.291 cm). The reliability based on means of three measurements was similar. The results were homoscedastic.

Conclusions The raters were able to measure the cross-sectional area of the rectus femoris muscle using RTU with good reliability across all the settings.

KEYWORDS

Muscle thickness; real-time ultrasonography; observer variation; reliability

Introduction

In humans, muscle mass remains relatively stable during early life, but after the age of 30, a natural process of muscle mass reduction begins at a rate of 0.5 to 1.0% per year [1]. With the aging process, the impaired balance between protein synthesis and proteolysis in skeletal muscle results in a progressive decline in skeletal muscle mass, strength, and function, which is referred to as sarcopenia [2]. On average, peak strength decreases by 20-40% between the ages of 30 and 80 [3].

Strength training is considered the most effective strategy for the prevention and treatment of sarcopenia [4]. Randomized controlled trials have shown positive effects of strength training on muscle mass, muscle strength, and physical performance [5, 6]. Gaining strength and muscle mass is a complex process that involves numerous factors, including strength training, proper nutrition, and sufficient rest [7]. Strength training involves the use of free weights, weight machines, or own body weight to overload the muscles and stimulate muscle growth [7]. To maximize the gains in strength and muscle mass, the strength training must be progressive and challenging [7].

The rectus femoris muscle is a vital component of the quadriceps group, serving as a powerful knee extensor and contributing to hip flexion [8]. Therefore, the rectus femoris plays an important role in maintaining lower limb stability and biomechanical control during activities such as walking, running, jumping, and stair climbing [8]. Both reduced quadriceps strength and decreased muscle thickness (cross-sectional area) of the rectus femoris measured by real-time ultrasonography (RTU) are associated with an increased risk of falls in older adults [9, 10]. The simultaneous assessment of muscle strength and size contributes to a more comprehensive understanding of muscle physiology and potential for improvement [9].

Assessment of reliability is a necessary first step in the validation process of clinical tests [11]. The reliability of RTU measurements is influenced by the standardization of anatomical location and pressure force applied during the assessment and possibly rater experience [12]. The reliability of the measurement has been evaluated in a series of studies, but their sample sizes were relatively small. The inter-rater reliability has been investigated in 12 healthy subjects by Takahashi et al. [13], in 15 healthy persons and 17 patients with chronic obstructive pulmonary disease by Hammond et al. [12], in 29 critically ill patients by Pardo et al. [14], and in 99 hospitalized patients by Pinto-Ramos et al. [15]. The inter-rater intra-class correlation coefficients (ICCs) point estimates ranged between 0.70 and 0.98 (relative reliability where 1 is perfect). Despite test-retest reliability being crucial for confirming the consistency of measurements over time, the evidence on the subject is very sparse. The inter-day ICC has been estimated to be 0.88 by Lima et al based on 15 healthy subjects [16] and 0.97 by Thomaes et al. based on 25 patients with coronary artery disease [17]. Therefore, we decided to conduct a new study featuring relative and absolute intra-rater, inter-rater, and inter-day reliability of the procedure in a larger sample.

Methods

The study was approved by the Human Research Ethics Committee of the Universidade Evangélica de Goiás (UniEvangélica), according to CEP opinion no. 6.210.982, with Certificate of Submission for Ethical Appraisal (CAAE) no.

69796523.7.0000.5076. Those who agreed to participate signed a Free and Informed Consent Form (TCLE), in accordance with resolution 196/96 of the National Health Council (CNS).

Subjects

The study included 106 participants of both sexes, aged between 18 and 73 with preserved cognitive ability and no other significant illness identified through a clinical history, blood pressure, and pulse measurements, physical examination, and complementary tests. They were recruited from the city of Anápolis – Goiás between August and December 2023.

Ultrasonography procedure

The ultrasonography procedure involved the use of a Mindray M6 ultrasound device equipped with a linear transducer (model L14-6Ns) operating at a frequency range of 6-14 megahertz (MHz). Two raters trained in RTU conducted the measurements, that is, a 36-year-old female biologist with a master's degree in human movement and rehabilitation (rater A) and a 28-year-old male physical educator with a master's degree in human movement and rehabilitation (rater B).

The participants were positioned supine on a stretcher with their legs fully extended and muscles relaxed for 10 minutes. Anatomical landmarks, including the greater trochanter and lateral epicondyle of the femur of the right thigh, were identified for each subject. The thickness of the rectus femoris muscle was analyzed at a point located 40% of the femur's length proximal to these landmarks. To ensure standardized distances between anatomical points and consistent transducer positioning, meticulous markings were made on the skin using a pen. During the procedure, a generous amount of ultrasound gel, soluble in contact water, was applied. The gel was directly applied to the transducer to minimize image distortion and facilitate the acoustic coupling necessary for accurate measurements. All sessions took place during the same period of the day in an air-conditioned room with only one rater present at the time. The raters were unaware of each other's results. Measurements were exclusively performed on the participants' right limbs. Each rater conducted three

measurements per subject during each visit, with two visits scheduled 7-10 days apart.

Statistics

Descriptive statistics were applied using IBM SPSS Statistics 29 and Microsoft Excel 2016.

Intra-rater reliability was estimated using the first and second measurements and inter-rater and inter-day reliability were estimated using the first measurements.

The relative rater reliability was calculated utilizing the ICC model two-way mixed with average measures and absolute agreement. The ICC values were interpreted as proposed by JC Nunnally and IH Bernstein [18]: ICC values of ≥ 0.900 represent good reliability.

Absolute reliability was calculated using within-subject standard deviation (S_w); the difference between a measurement and the true value can be expected to be less than $1.96 \cdot S_w$ for 95% of observations. The Minimal Detectable Difference (MDD) in centimeter MT that must be exceeded to be 95% confident that a real change has occurred between measurements was estimated using the formula $S_w \cdot 1.96 \cdot \sqrt{2}$ [19]. The distribution of data was inspected using Bland-Altman plots with means and differences of paired measurements and 95% limits of agreement [20].

Results

The characteristics of the participants are described in Table 1. The mean MT was 2.12 cm. The intra-rater ICC for raters A and B was 0.998 at both visits (MDDs = 0.074-0.082 cm). The inter-rater ICC was 0.976 at visit 1 and 0.977 at visit 2 (MDDs = 0.269-0.270 cm). The inter-day ICC was 0.973 for rater A and 0.972 for rater B (MDDs = 0.286-0.291 cm) (Table 2). The results were homoscedastic according to

the Bland-Altman plots (Figure 1-8). Shifting the analysis approach based on single measurements to means of three measurements did not change the reliability estimates meaningfully (Table 2).

Table 1 Sex, age, and rectus femoris muscle thickness of the participants.

	Females (N = 58)		Males (N = 48)		Both sexes (N = 106)	
	Age (years)	MT (cm)	Age (years)	MT (cm)	Age (years)	MT (cm)
Mean	29.91	1.86	36.00	2.43	32.67	2.12
Min-max	18-73	0.89-2.68	18-67	1.51-3.25	18-73	0.89-3.25
SD	14.00	0.32	14.08	0.38	14.27	0.38

The numbers for MT are based on measurement 1 and 2 by both raters. MT = muscle thickness; SD = standard deviation.

Table 2 Reliability results – agreement between single measurements and between means of measurements.

Rater	ICC (95% CI)	Mean (cm)	95% CI of true value (cm)	MDD (cm)
Intra-rater reliability – agreement between 1. and 2. measurements – visit 1				
A	0.998 (0.996-0.999)	2.089	±0.054	0.077
B	0.998 (0.997-0.999)	2.128	±0.056	0.079
Intra-rater reliability – agreement between 1. and 2. measurements – visit 2				
A	0.998 (0.998-0.999)	2.100	±0.052	0.074
B	0.998 (0.997-0.998)	2.146	±0.058	0.082
Inter-rater reliability – agreement between 1. measurements – visit 1				
AB	0.976 (0.963-0.984)	2.114	±0.191	0.270
Inter-rater reliability – agreement between means of 3 measurements – visit 1				
AB	0.978 (0.967-0.985)	2.107	±0.181	0.256
Inter-rater reliability – agreement between 1. measurements – visit 2				

AB	0.977 (0.964-0.985)	2.125	± 0.190	0.269
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Inter-rater reliability – agreement between means of 3 measurements – visit 2

AB	0.977 (0.962-0.985)	2.120	± 0.189	0.267
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Inter-day reliability – agreement between 1. Measurements

A	0.973 (0.961-0.982)	2.101	± 0.206	0.291
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B	0.972 (0.958-0.981)	2.138	± 0.202	0.286
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Inter-day reliability – agreement between means of 3 measurements

A	0.976 (0.964-0.983)	2.094	± 0.196	0.277
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B	0.973 (0.961-0.982)	2.133	± 0.196	0.278
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CI = Confidence Interval; ICC = Intraclass Correlation Coefficient; MDD = Minimal Detectable Difference.

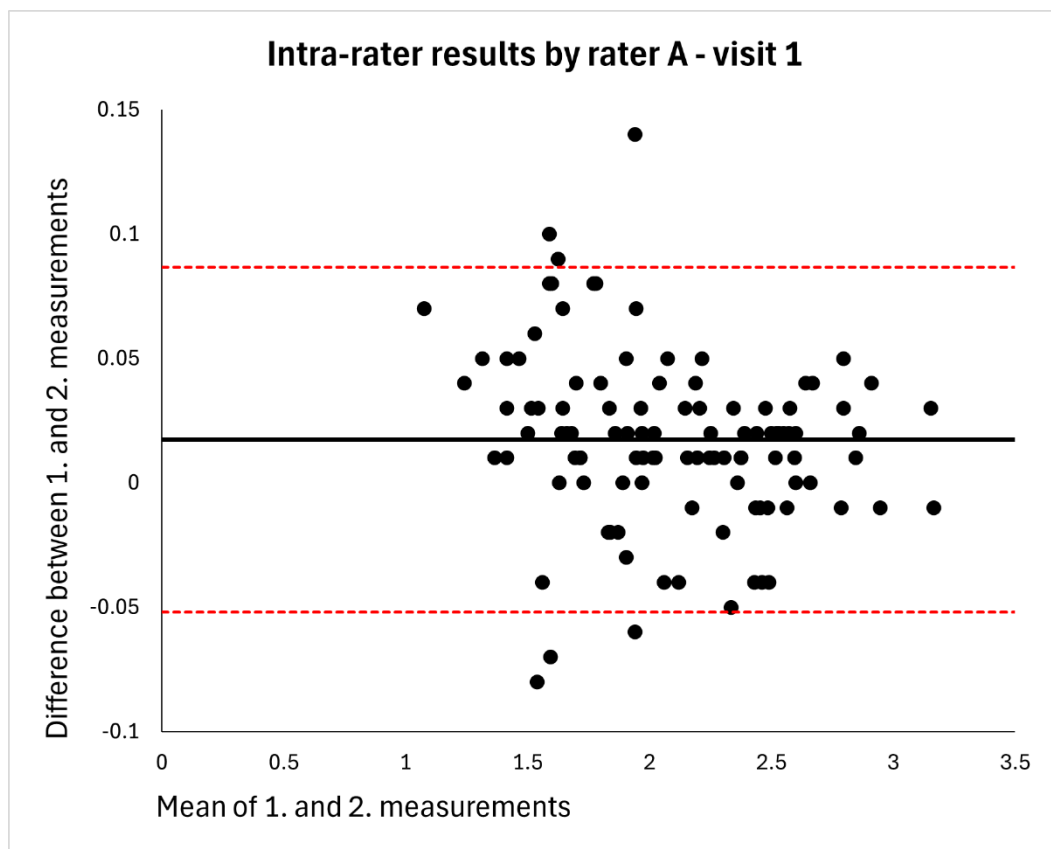


Figure 1 Level of agreement between rater A's 1. measurements at visit 1

Note. The values are cm. The thick horizontal solid line represents the mean difference and the dotted horizontal lines represents the 95% limits of agreement.

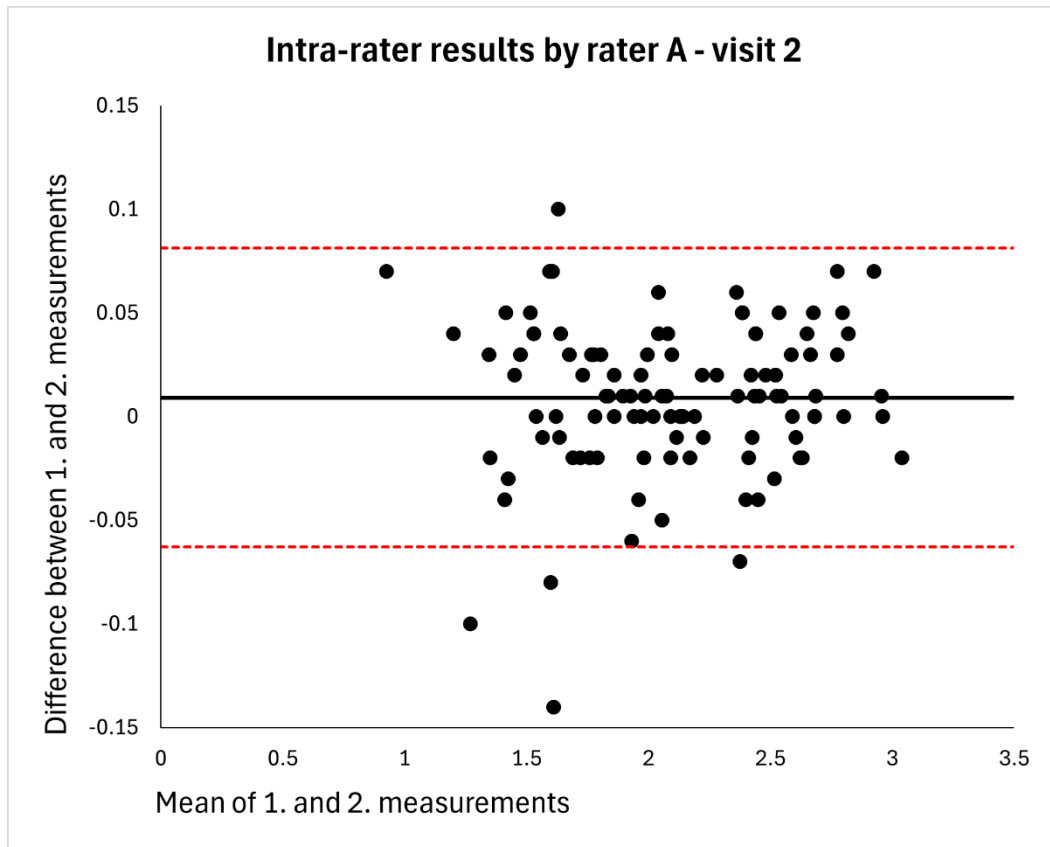


Figure 2 Level of agreement between rater A's 1. measurements at visit 2

Note. The values are cm. The thick horizontal solid line represents the mean difference and the dotted horizontal lines represents the 95% limits of agreement.

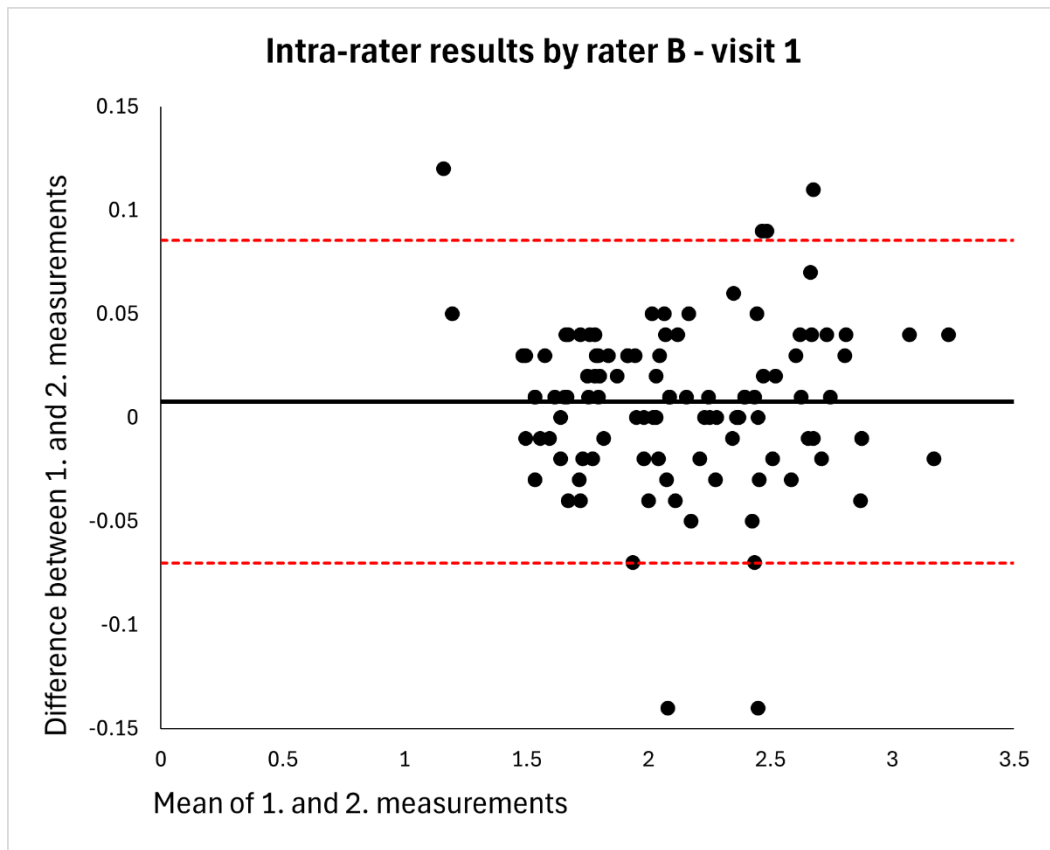


Figure 3 Level of agreement between rater B's 1. measurements at visit 1

Note. The values are cm. The thick horizontal solid line represents the mean difference and the dotted horizontal lines represents the 95% limits of agreement.

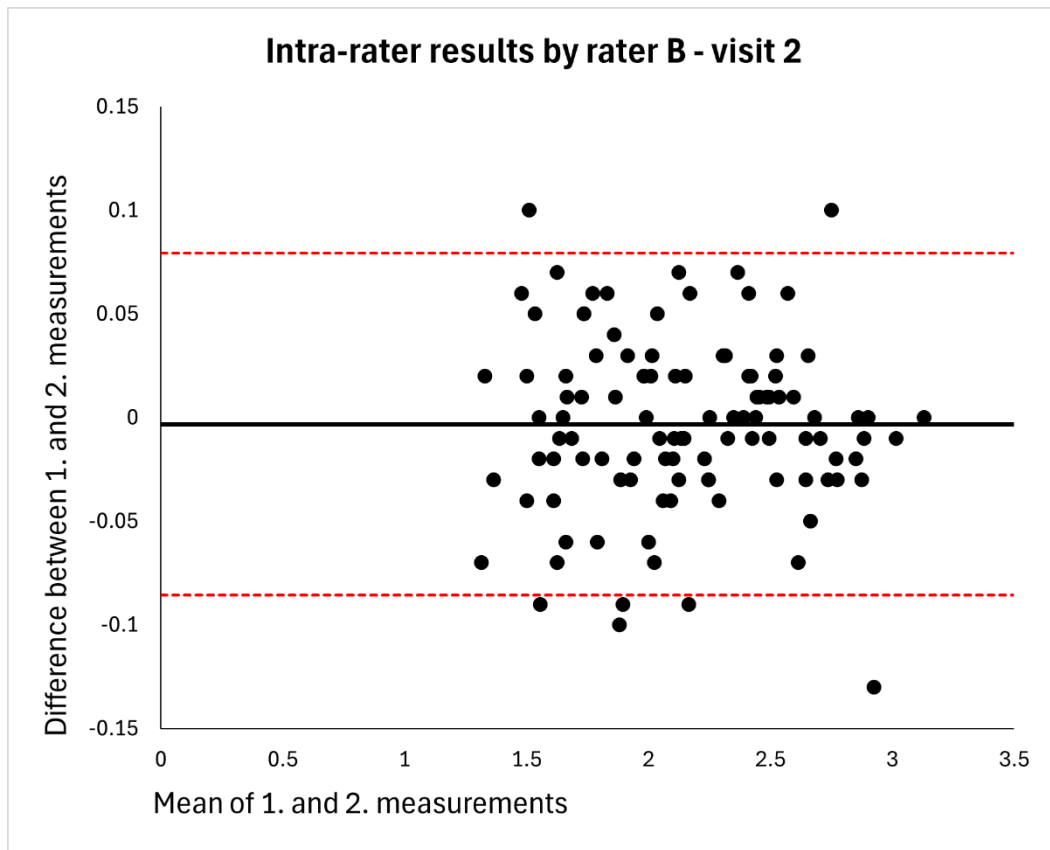


Figure 4 Level of agreement between rater B's 1. and 2. measurements at visit 2

Note. The values are cm. The thick horizontal solid line represents the mean difference and the dotted horizontal lines represents the 95% limits of agreement.

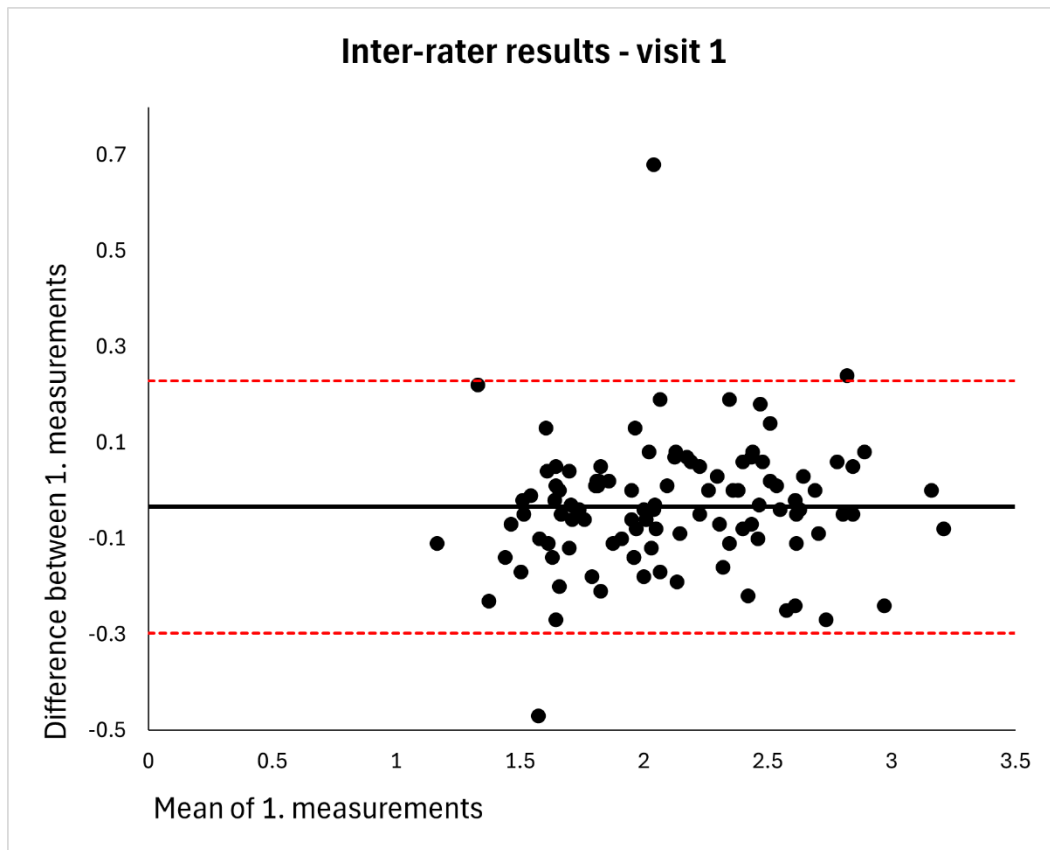


Figure 5 Level of agreement between rater A's and B's 1. measurements at visit 1

Note. The values are cm. The thick horizontal solid line represents the mean difference and the dotted horizontal lines represents the 95% limits of agreement.

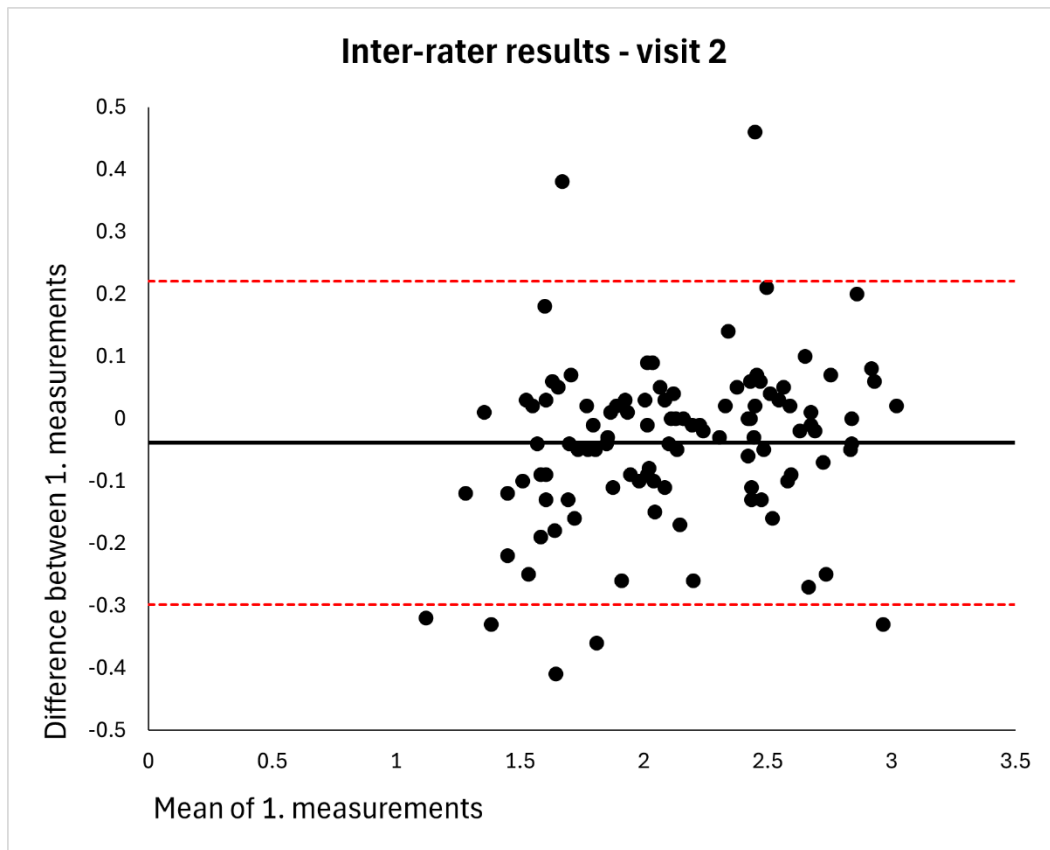


Figure 6 Level of agreement between rater A's and B's 1. measurements at visit 2

Note. The values are cm. The thick horizontal solid line represents the mean difference and the dotted horizontal lines represents the 95% limits of agreement.

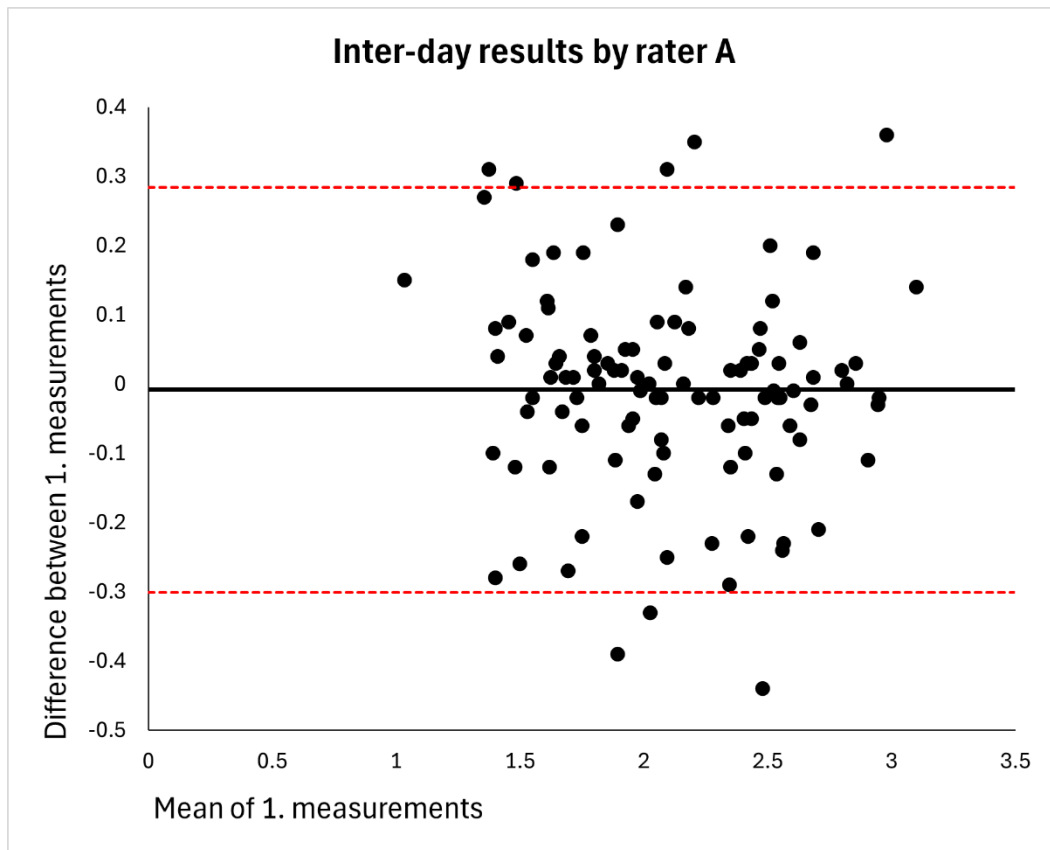


Figure 7 Level of agreement between rater A's 1. measurements at visit 1 versus at visit 2

Note. The values are cm. The thick horizontal solid line represents the mean difference and the dotted horizontal lines represents the 95% limits of agreement.

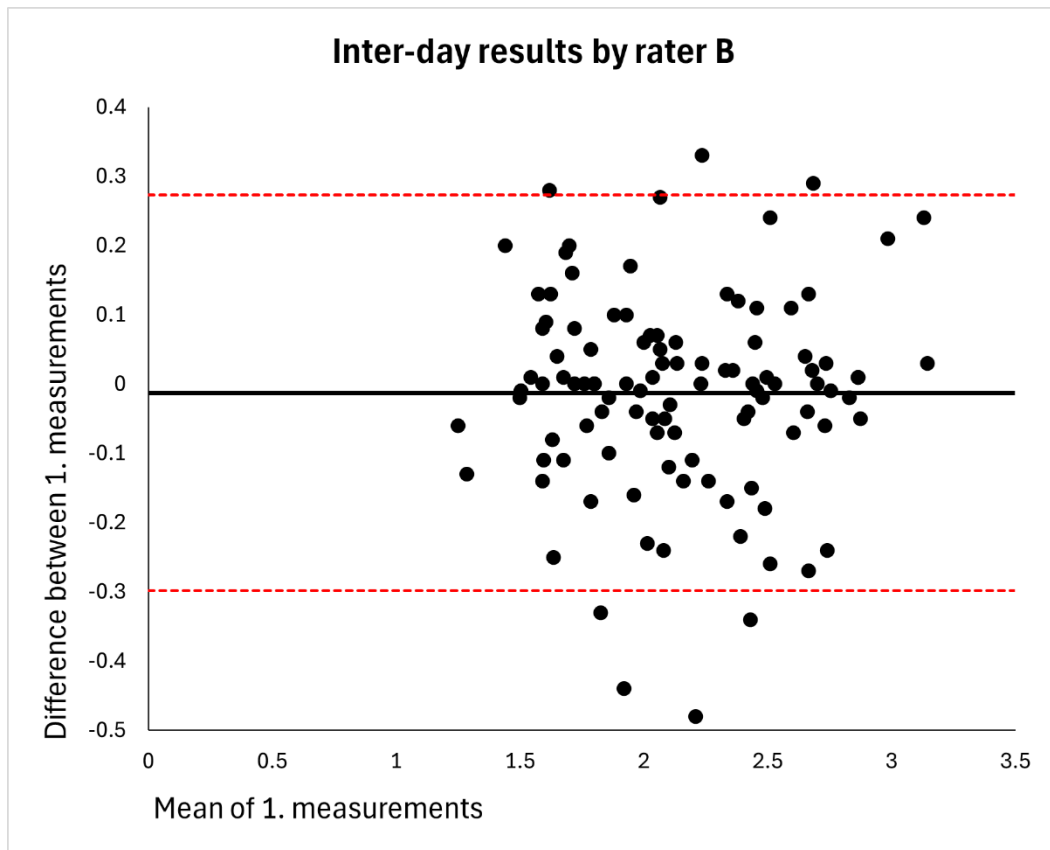


Figure 8 Level of agreement between rater B's 1. measurements at visit 1 versus at visit 2

Note. The values are cm. The thick horizontal solid line represents the mean difference and the dotted horizontal lines represents the 95% limits of agreement.

Discussion

In this study, a 36-year-old female biologist with a master's degree in human movement and rehabilitation and a 28-year-old male physical educator with a master's degree in human movement and rehabilitation assessed the rectus femoris MT in healthy persons using RTU to estimate the intra-rater, inter-rater, and inter-day reliability of the procedure. The raters had extensive experience with RTU and followed a standardized protocol. The relative reliability was good across all the settings. Compared with the mean MT of both sexes, the intra-rater MDD corresponded to 3.5-3.7% of the MT, the inter-rater MDD corresponded to 12.7-12.8% of the MT, and the

inter-day MT corresponded to 13.4-13.9% of the MT. The percentages were slightly higher for females and lower for males due to the greater MT in males. Whether the measurement errors are adequate depends on the context in which the measurements are being used, including the analytical goals of the user [21, 22]. It is our interpretation that RTU may serve as a valuable adjunct to strength tests by providing additional insight into muscle morphology and health, facilitating a more comprehensive assessment of muscular function and guiding personalized strength training interventions [9]. We estimated the reliability based on both single measurements and means of three consecutive measurements, but the results did not vary meaningfully. In contrast to our findings, Hammond et al. [12] and Takahashi et al. [13] found that the relative inter-rater reliability of the procedure in healthy subjects was only acceptable. Similarly, Lima et al. [16] reported that the relative inter-day reliability is only acceptable. The discrepancies may be a result of the smaller sample sizes in the three studies (106 versus 12-15 healthy subjects), that is, random error. Variation in rater experience is another plausible explanation [12]. Our inter-rater ICC values are also higher than in studies on the topic that included patients [12, 15, 17]. However, it is essential to recognize that ICC values may fluctuate depending on the specific models utilized, and the models used have rarely been reported in studies on the matter. We chose the ICC two-way mixed model, assuming the raters were fixed and the subjects were random samples from a larger population [23]. Our ICC results in healthy individuals likely extend to patients because both groups share similar physiological muscle characteristics and the methodology of RTU is consistent across populations.

The costs associated with RTU assessment include the purchase of the machinery, ultrasound gel, and training of personnel. Although the initial cost of purchasing a RTU device may seem significant, research suggests that it often leads to long-term

cost savings by eliminating additional diagnostic testing [24].

Limitations of the study

Since our study solely included raters experienced with the procedure, it is unclear whether the results can be translated to less experienced raters. Therefore, we warrant future studies on the topic assessing the reliability using raters with different levels of experience with RTU.

Conclusions

The two raters were able to assess the rectus femoris MT with good intra-rater, inter-rater, and inter-day ICCs using RTU in healthy persons. Our results indicate that the procedure is suitable for this purpose when applied by experienced raters.

Abbreviations

CI: confidence interval; ICC: interclass correlation coefficient; MDD: minimal detectable difference; MHz: megahertz; MT: muscle thickness; RTU: real-time ultrasonography; SD: standard deviation; Sw: within-subject standard deviation

Acknowledgements

None.

Authors' contributions

KRS (rater A) and PAI (rater B) performed the ultrasonography. MBS conducted the statistical analyses. The results were interpreted by all the authors (MBS, KRS, PAI, ASSF, PSLLM, JMB, PSL, and RABLM). MBS and RABLM drafted the initial manuscript. Subsequent revisions were made by MBS, based on significant feedback from

KRS, PAI, ASSF, PSLLM, JMB, PSL, and RABLM. All the authors read and accepted the final version of the manuscript.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the Human Research Ethics Committee of the Universidade Evangélica de Goiás (UniEvangélica), according to CEP opinion no. 6.210.982, with Certificate of Submission for Ethical Appraisal (CAAE) no.

69796523.7.0000.5076. Those who agreed to participate signed a Free and Informed Consent Form (TCLE), in accordance with resolution 196/96 of the National Health Council (CNS).

Consent for publication

Not applicable.

Declaration of interests

The authors declared that there is no conflict of interest.

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9.3 Anexo 3 - Applications of Pulsed Electromagnetic Field Therapy in Skeletal-Muscle System: An Integrative Review



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REVIEW

Applications of Pulsed Electromagnetic Field Therapy in Skeletal-Muscle System: An Integrative Review

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ABSTRACT

Background: The Pulsed Electromagnetic Field (PEMF) technology has attracted increasing interest since consistent evidence of its therapeutic properties has been demonstrated to treat musculoskeletal conditions. However, this technology is not new, and has already been used in different experimental models and clinical studies for the treatment of tendinopathies, osteoarthritis, increased cell proliferation, bone consolidation, among others. **Methods:** In this work, we carried out an integrative review of clinical and experimental studies published in the last twenty years, on the available scientific evidence that demonstrate the effects of PEMF in different applications for health treatments. Five databases including Medline, Pubmed Central, Scopus, Lilacs and PEDro were searched for studies from 2001 to September 2022. The results were analyzed by the team of researchers and clinical professionals to assure methodological quality of the studies for the elaboration of the theoretical review on the effects of electromagnetic field stimulation on skeletal muscles, tendon or bones. **Results:** Sixty-two studies were included in this review, presenting evidence of the biological effects of PEMF that can suggest it's possible use to treat different disorders. **Conclusions:** Pulsed electromagnetic fields (PEMF) present relevant clinical and experimental evidence of beneficial effects in the treatment of several musculoskeletal inflammatory disorders, such as tendinopathies and osteoarthritis, in addition to the treatment of urinary incontinence and abdominal diastasis. PEMF can be considered as the evolution of electrical currents for the treatment of musculoskeletal disorders, mainly due to its better tolerance by patients.

Keywords: Tendinopathies; Osteoarthritis; PEMF; Pulsed electromagnetic field; Skeletal muscle; Urinary incontinence; Abdominal diastasis.

BACKGROUND

The original concept of electromagnetic induction was described by Faraday in 1831, one of the strongest contributions to the study of electromagnetism⁽¹⁾. His discoveries encompass the basic principles of electromagnetic induction, diamagnetism, and electrolysis⁽¹⁾. He is considered one of the most influential scientists of all time. Briefly, a coil of wire generates an intense alternating magnetic field, which consequently induces a secondary electrical current in the tissue base where it interacts with neurons⁽²⁾. The Faraday-Neumann-Lenz law, or Faraday's law of induction, is one of the basic equations of electromagnetism. Mathematical expressions describe and predict how the magnetic field interacts with the electric field and, as a result, the interaction of these forces produces another force called the electromotive force: electromagnetic induction.

The Electromagnetic Wave is a very complex form of interaction, of interlace of the two, apparently distinct phenomena of electricity and magnetism that were studied as separate fields for decades. In 1819 Oersted said that electric charges in motion create magnetic effects. Theoretical models were created to explain the properties of magnets through the movement of electric charges, including the Earth's magnetic field. The theory of Maxwell was able to

predicts that if an electric charge moves with a variable speed, oscillating or rotating, then it would create an electric field whose temporal variation is not constant, and consequently the magnetic field was not also constant.

One of the important differences between the well-known electrical currents used in health sciences for treatments, is that the wires propagate linearly from one electrode to the other, and the electromagnetic wave that propagates in 3 axes, or three-dimensionally, generating what we call an electromagnetic field. Theoretically, the electromagnetic field appears significantly more effective in recruiting muscle fibers and producing muscle contraction.

Figure 01 illustrate an electrical current, showing that hypothetically, the electrons move superficially in the skeletal muscles, in a linear fashion, from one pole to the other, that is, from one electrode to the other, according to polarity. We can observe that the skeletal muscle contraction produced by the current is not maximal. In fact, an electrical current capable of producing a maximum muscle contraction would certainly be harmful, or with a high probability of intercurrents such as an electrical burn. Furthermore, the feeling of an electric shock would certainly be unbearable for the patient.

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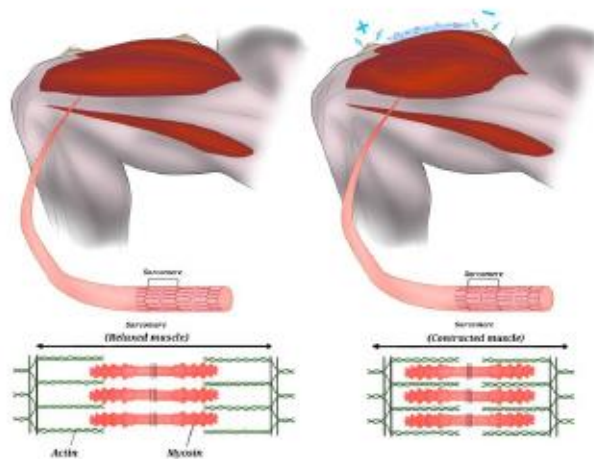


Figure 01: Schematic representation of the effects of electrical currents on skeletal muscle. The illustration shows the electric current acting more superficially on the musculature, causing a submaximal muscle contraction.

Figure 02 illustrate an application of Pulsed electromagnetic field, that potentially evolves the whole muscle, being able to recruit the muscle and to promote maximal muscle contraction. Besides, PEMF does not

produce the sensation of electric shock, being significantly more bearable for the patient, especially if we consider elderly individuals.

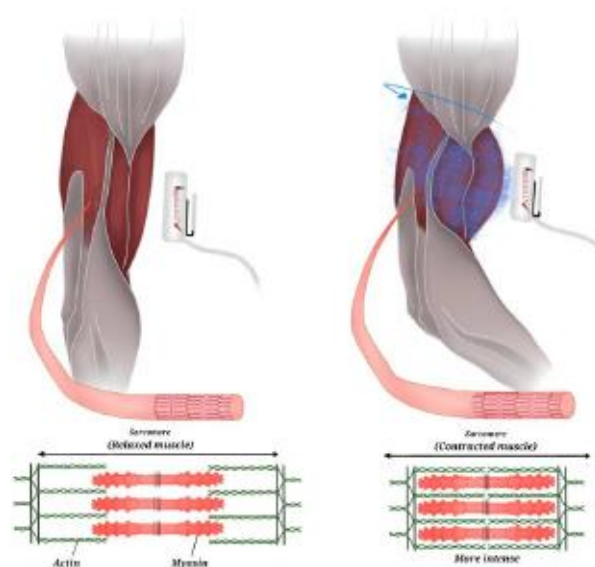


Figure 02: Schematic representation of the effects of PEMF on skeletal muscle contraction. The illustration shows the PEMF acting deeply on the muscle, due to its 3D effect, causing a supramaximal muscle contraction.



The pulsed electromagnetic field (PEMF) uses alternating magnetic fields, based on the law of electromagnetic induction, promotes electrical currents that depolarize the neuromuscular tissue may resulting in supramaximal contractions^[3,4]. Motor neurons are activated due to their large diameter and therefore less resistance compared to other types of neurons. Since nociceptors are not activated, the application of magnetic stimulation is not painful^[5]. This is an important point since the classic discomfort of therapeutic electrical currents does not exist with PEMF.

The new PEMF equipment normally comprises a circular coil located in the applicator, which is placed over the treatment area. Starting a treatment, an alternating electric current run into the circular coil and the alternations in the electric current induce rapidly changing magnetic waves which propagate into the underlying tissue, inducing consequently a secondary electric current that will depolarize the muscle-innervating motor neurons and induce muscle contractions.

Under normal conditions, the greatest amount of tension that could be developed and performed physiologically is called maximal voluntary contraction (MVC)^[2]. It usually only lasts for a fraction of a second. Contractions with tension greater than MVC are defined as supramaximal contractions^[6]. PEMF possesses the ability to generate sustained supramaximal contractions for several seconds, which significantly increases stress/workload, if muscle adaptation takes place. In supramaximal contraction, proteins are degraded, but amino acids are reused in the synthesis process at the expense of intense energy expenditure^[7].

However, the evolution of research has demonstrated that besides the muscle stimulations, PEMF are able to interact with different structures of the locomotor system, including tendons, cartilage and bones. The purpose of the present work was to carry out a narrative review with a systematic methodology of bibliographic search, about the applications of PEMF technology in the musculoskeletal system.

Search Strategy

Five databases including Medline, Pubmed Central, Scopus, Lilacs and PEDro were searched for studies from 2001 to September 2022.

Keywords and MeSH terms were used and combined by Boolean operators as follows: (PEMF OR HIFEM AND Skeletal muscle OR muscle OR bone OR tendon; Pulsed Electromagnetic Field AND Skeletal muscle OR muscle OR bone OR tendon; The results were analyzed by the team of researchers and clinical

professionals for the elaboration of the theoretical review on the effects of electromagnetic field stimulation on skeletal muscles, tendon or bones.

Pulsed Electromagnetic Field (PEMF) and Tendon Diseases

Tendinopathies are part of the so-called group of the most common musculoskeletal diseases in modern society. There are several causes, whether due to daily activities, work-related or even repetitive movements or overcharge in sports. Chronic pain in the tendons is relatively common, especially considering the Achilles, patellar and elbow tendons^[8]. Tendinopathies are changes in the health of the tendon, which are generally frequent and difficult to treat, disabling professional and recreational athletes as well as ordinary people in their workplaces^[9]. The high prevalence, along with the fact that they often become chronic, make these diseases a major socio-economic problem where medical interventions and therapies for rehabilitation are limited^[10].

The PEMF technology has attracted increasing interest since consistent evidence of its therapeutic properties has been demonstrated to treat musculoskeletal conditions. Concerning on tendon disorders, some scientific studies have investigated the efficacy of PEMF in tendon healing. In vivo studies showed that PEMFs was able to improve tendon healing through a reduction of inflammation, improvement of mechanical properties and an induction of faster collagen alignment. Taken together, these results suggest a reparative role PEMFs in tendinopathies^[11].

De Girolamo et al^[12,13] demonstrated as cytokines (interleukin (IL)-6 and IL-10) and growth factor (TGF- β) release and up-regulation of tenogenic gene transcription (scleraxis and type I collagen) in response to PEMF. A dose-dependent response of human TCs to PEMFs (1.5 mT, 75Hz) was observed.

Rosso et al^[14] also demonstrated with in vitro studies on human tendon cells an increased cell proliferation after PEMF stimulation. According to Randelli et al^[15], the possibility of activating tendon healing through electromagnetic stimulation has become increasingly popular. However, the mechanisms of beneficial effects are not elucidated. The authors suggest the possibility of stem cells involvement in the healing process. The effects of electromagnetic fields were analyzed in human tendon stem cells isolated from patients undergoing surgeries and the treatment presented positive effects on stem cell marker expression, as treated cells maintained a higher expression of these markers during culturing.





Kamel et al⁽¹⁶⁾ compared the effects of Pulsed Electromagnetic Field with traditional Ultrasound in the treatment of postnatal carpal tunnel syndrome in a randomized controlled clinical trial in Egyptian women. In this study, one of the groups was treated with pulsed electromagnetic field, with nerve and tendon gliding exercises for the wrist, three times per week for four weeks. The second group was treated with pulsed ultrasound and wrist exercises. The authors evaluated pain level, sensory and motor distal latencies and conduction velocities of the median nerve, functional status scale and hand grip strength pre- and post-treatment. The authors observed a significant reduction of pain levels and sensory and motor distal latencies of the median nerve. Besides, they also observed an increase in sensory and motor conduction velocities of the median nerve as well as in the hand grip strength in both groups. However, a significant difference between the two groups in favor of pulsed electromagnetic field treatment was reported. The symptoms were alleviated in both groups, but significantly more effective for PEMF than for pulsed ultrasound, at least in treating postnatal carpal tunnel syndrome.

Tucker et al⁽¹⁷⁾ showed that PEMF positively affected the biomechanical properties and tendon healing and does not alter joint function in a rat rotator cuff repair model (rotator cuff tendons). This is a very important study considering that Rotator cuff tears are common musculoskeletal injuries which often require surgical intervention and post-repair prognosis is poor, with surgical repairs that fail in up to 94% of cases.

Liu et al⁽¹⁸⁾ studied the effects of PEMF on tenocytes and muscle cells to define the role of a commercially available PEMF on tenocytes and myoblasts growth and differentiation in vitro. The authors demonstrated that 2 weeks treatment of PEMF enhanced gene expressions of growth factors in human rotator cuff tenocytes under inflammatory conditions. PEMF significantly enhanced C2C12 myotube formation under normal and inflammatory conditions. This study suggests PEMF seems to have a positive activity inducing tenocyte gene expression and myoblast differentiation thus potentially serving as a non-surgical treatment to improve rotator cuff tendon lesions.

Huegel et al⁽¹⁹⁾ demonstrated that PEMF improved the rotator cuff tendon-to bone healing. These findings suggest that PEMF can serve as an adjuvant therapy to improve rotator cuff tendinitis. In 2015, Osti et al⁽²⁰⁾ in a randomized clinical trial demonstrated that PEMF therapy is effective in reducing inflammation, swelling and pain after rotator cuff arthroscopic repair.

In rats, Gehwolf et al⁽²¹⁾ recently demonstrated that the exposure to high energy PEMF treatment in

inflamed condition affected different biological mechanisms such as extracellular matrix remodeling, inflammation and negative regulation of apoptosis.

Vinhas et al⁽²²⁾ investigated the modulatory effect of pulsed electromagnetic field (PEMF) on the inflammatory profile of human tendon-derived cells after stimulation with interleukin-1 β . The PEMF technology was investigated varying the frequency, intensity (1.5, 4, or 5 mT), and duty-cycle (10% or 50%) in cell cultures of Human tendon cells. The authors reported that PEMF was effective in reducing IL-6 and TNF- α production besides the gene expression of TNF α , IL-6, IL-8, COX-2, and metalloproteinases MMP-1, MMP-2, and MMP-3. On the other hand, anti-inflammatory mediators IL-4, IL-10, and TIMP-1 expression were increased. The in vitro results reinforce the hypothesis of anti-inflammatory action of PEMF in tendon tissues.

Colombini et al⁽²³⁾ investigated the anabolic and anti-inflammatory PEMF-mediated response on Tendon cells in an in vitro model of inflammation. Besides, the authors also investigated the possible role of Adenosine receptors on the anti-inflammatory effect of PEMF in tendon cells. They concluded that Adenosine receptors (A2ARs) have a role in the promotion of the Tendon cells anabolic/repairative response to PEMFs.

Recently, Dolkart et al⁽²⁴⁾ also studied the effects of the continuous pulsed electromagnetic field (PEMF) on rotator cuff (RC) healing using a rat model. In their study, the authors hypothesized that PEMF application after rotator cuff detachment and repair could produce beneficial effects on biomechanical properties, tissue morphology and bone density. The authors concluded that PEMF was able to enhance early postoperative tendon-to-bone healing in an acute rat supraspinatus detachment and repair model besides an increased biomechanical elasticity and better collagen organization, suggesting an improvement of the rotator cuff healing.

Pulsed Electromagnetic Field (PEMF) and Joint Diseases

Osteoarthritis (OA) is a burden to the modern society. A common and disabling condition that represents a challenge to the public and private health systems representing significant socioeconomic costs and complex implications for the patients^(25,26). Osteoarthritis is highly prevalent in elderly population. According to Iwasa and Reddi⁽²⁷⁾, more than 30 million are currently affected with increasing tendencies.

Together with orthopaedic trauma, tendon and ligament lesions, ageing and increasing obesity in the world population, OA is becoming more prevalent, with worldwide estimates suggesting that 250 million suffers with this painful condition. According to the



scientific literature, the majority of OA patients do not receive appropriate management therapies. Management therapy is characterized as mainly by rest, exercise and NSAID's. However, moderate evidence for electrophysical agents, such as photobiomodulation⁽²⁸⁻³¹⁾ has been demonstrated.

The medical cost of osteoarthritis in developed countries has been estimated to account for between 1% and 2-5% of the gross internal product (GIP) with hip and knee joint replacements representing the major proportion of these costs. Besides the direct costs, the indirect costs represented by work loss and premature retirement are also substantial and frequently underestimated or even forgotten⁽³²⁾.

Pulsed Electromagnetic Field therapy has also been suggested as an alternative treatment for OA⁽³³⁾. According to Shupak et al⁽³⁴⁾, PEMF promotes joint benefits based on basic principles of physics: Wolff's law, the piezoelectric properties of collagens, and the concept of streaming potentials. Although the effects of PEMF have previously been reported to increase morphogens and promote osteogenesis^(35,36), the real therapeutic effects of PEMF on osteoarthritis still on debate.

Osteoarthritis is a whole joint disease, involving structural alterations in the hyaline articular cartilage, subchondral bone, ligaments, capsule, synovium, and periarticular muscles⁽³⁷⁾. The complex pathogenesis of osteoarthritis involves mechanical, inflammatory, and metabolic factors, which ultimately lead to structural destruction and failure of the synovial joint. The disease is an active dynamic alteration arising from an imbalance between the repair and destruction of joint tissues, and not a passive degenerative disease or so-called wear-and-tear disease as commonly described. In this context the needing for cartilage stimulating therapies is highly necessary.

During the osteoarthritis process, cartilage composition changes and the cartilage loses its integrity⁽³⁸⁾. Proliferating synoviocytes also release proinflammatory products which are accompanied by tissue hypertrophy and increased vascularity. In the subchondral bone, bone turnover is increased, and vascular invasion takes place, going from the subchondral bone, through the tidemark, and into the cartilage. One of the main goals of OA treatment is to regenerate a native articular cartilage, including a low friction coefficient.

Pulsed Electromagnetic Field (PEMF) and Cartilage

The use of PEMF as an adjunctive therapy for joint diseases is not exactly new. PEMF has been studied

for at least 20 years for Muscle-skeletal and joint disorders. In 2005, the first clinical trial that we were able to identify⁽³⁹⁾ enrolled 83 patients in a placebo-controlled study. The authors reported that they were unable to demonstrate a beneficial symptomatic effect of PEMF in the treatment of knee OA in all patients. However, in patients younger than 65 years old, there were significant and beneficial effect of treatment related to stiffness.

Fini et al⁽⁴⁰⁾, studied the pulsed electromagnetic field stimulation on knee cartilage, subchondral and epiphyseal trabecular bone of aged Dunkin Hartley guinea pigs. PEMF stimulation significantly changed the progression of OA lesions in all examined knee areas, even in the presence of severe OA lesions.

van Bergen et al⁽⁴¹⁾ published a clinical trial protocol consisting of prospective, double-blind, randomized, placebo-controlled trial (RCT) to be conducted in five centers throughout the Netherlands and Belgium. 68 patients would be randomized to either active PEMF-treatment or sham-treatment for 60 days, four hours daily. However, only in 2016 the results of the Clinical Trial were published⁽⁴²⁾. PEMF does not lead to a higher percentage of patients who resume sports or to earlier resumption of sports after arthroscopic debridement and microfracture of talar OCDs. Furthermore, no differences were found in bone repair between groups.

In 2013, Chen et al⁽⁴³⁾ studied the effects of electromagnetic fields on adipose-derived (ADSC) stem cells in a chondrogenic microenvironment in vitro. Interestingly, PEMF treatment increased mineralization of ADSC and enhanced chondrogenic differentiation of ADSCs cultured in a chondrogenic microenvironment. PEMF enhanced both osteogenesis and chondrogenesis under the same conditions.

Veronesi et al⁽⁴⁴⁾ demonstrated that that PEMF stimulation can be used as adjuvant therapy to preserve cartilage from detrimental effects of high inflammatory cytokine levels during OA. PEMFs were able to counteract the progression of OA acting on both cartilage cellularity and ECM in cartilage previously treated with IL1 β . The experimental model consisted of culturing bovine cartilage explants with a high dose of interleukin 1 β (IL1 β , 50 ng/ml) at different experimental times (24 h, and 7 and 21 days). The effects of PEMFs (75 Hz, 1.5 mT) were evaluated in cartilage explants treated with IL1 β or not (control), in terms of cartilage structure, cellularity and proteoglycans, glycosaminoglycans, collagen II and transforming growth factor β 1 synthesis by using histology, histomorphometry and immunohistochemistry.





Bagnato et al^[40] performed an important randomized, double-blinded and placebo-controlled clinical trial with sixty-six OA patients. In this study, patients with radiographic evidence of knee OA and persistent pain higher than 40 mm (VAS) were recruited. The clinical trial consisted of 1 month treatment in 60 knee OA patients. The primary outcome was the reduction in pain intensity and the secondary outcomes included quality of life assessment (SF-36 v2), pressure pain threshold (PPT) and changes in intake of NSAIDs/analgesics. The authors reported that PEMF was effective to reduce pain in knee OA patients and also improved pain threshold and physical functioning. Besides, twenty-six per cent of patients in the PEMF group stopped taking NSAIDs or any other analgesic drug, and no adverse events were detected.

Yang et al^[41] investigated the efficacy of pulsed electromagnetic field (PEMF) treatment on cartilage and subchondral trabecular bone in knee osteoarthritis (OA) using an experimental model induced by low-dose monosodium iodoacetate in rats. The authors observed that PEMF treatment increased bone and cartilage formation, and decreased bone and cartilage resorption, suggesting that PEMF might become a potential biophysical treatment modality for osteoarthritis.

Zhou et al^[42] investigated the effects of pulsed electromagnetic field on cartilage degeneration, and expression of mitogen-activated protein kinases (MAPKs) and matrix metalloproteinases (MMPs), in an experimental rat model of osteoarthritis induced by anterior cruciate ligament transection. The authors performed histological examination, enzyme-linked immunosorbent assay, quantitative real-time polymerase chain reaction, to assess cartilage degeneration, urine C-terminal cross-linking telopeptide of type II collagen (CTX-II), and mRNA expression of extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (c-Jun), p38, and MMPs and the conclusions were that PEMF may regulate the catabolic factor, MMP13, and inhibit cartilage destruction, at least partially, by inhibiting MAPKs signaling pathway.

Recently Parate et al^[47] demonstrated that PEMF stimulation was able to modulate paracrine function of mesenchymal stem cells (MSCs) for the enhancement and re-establishment of cartilage regeneration in states of cellular stress.

According to Varani et al^[48], the application of PEMFs in tissue repair is indicated to improve the functional and mechanical properties of the engineered construct and to favor graft integration in bones. Besides, PEMF is indicated to control the local inflammatory response, and to foster tissue repair from both implanted and resident MSCs cells. Vinod et al^[49]

demonstrated in vitro that PEMF was able to induce chondrogenesis.

Yang et al^[20] recently showed that PEMF attenuates structural and functional progression of OA through inhibition of TNF- α and IL-6 signaling. These results are significant since chondrocyte death is regulated by TNF- α and IL-6 signaling.

According to Li Y et al^[24], PEMF treatment was proven to enhance the quality of engineered chondrogenic constructs in vitro and facilitate chondrogenesis and cartilage repair in vivo. Liu J et al^[52] demonstrated that PEMF alleviated the degree of inflammation and degeneration of cartilage in rats with OA, based on the histopathological changes and decline of the expression of IL-1 β and MMP-13. The authors suggest that PEMF could be a highly promising noninvasive strategy to slow down the progression of OA.

PEMF and Muscle Hypertrophy

According to Duncan et al^[33], in an in vivo study carried out in a porcine experimental model, PEMF was capable of inducing hypertrophic muscle alterations after 2 weeks of treatment. The authors report an increase in muscle mass density of 20.56%. In the same study, an increase in muscle fiber density (hyperplasia) of 8.0% was observed. Mean individual muscle fiber size increased by 12.15% 2 weeks after treatment, while the control group showed no significant changes in fiber density or hyperplasia. The authors suggest that PEMF can be used for non-invasive induction of muscle growth.

The exact mechanism of muscular contraction by the electromagnetic field remains unknown. The classic hypothesis is that of depolarization of peripheral motor neurons, with release of acetylcholine in the myoneural plate. Acetylcholine binds to receptors on the membrane of skeletal muscle cells (Sodium Receptor Channels), changing the membrane voltage and inducing the opening of voltage-gated calcium channels, resulting in a massive influx of calcium and inducing muscle contraction. However, there are evidence that PEMF is able to stimulate at least two molecular mechanisms related to the expression of Voltage-dependent Calcium Channels and increase of intracellular calcium concentrations in bone tissue. However, the effect observed in bone cells may be repeating itself in muscle tissue, which would explain the greater effectiveness of PEMF in relation to electrical currents. This is because, the effect of muscle contraction, in fact, can be triggered by a direct change in voltage of the membrane of the skeletal muscle cell, leading to the opening of voltage-gated calcium channels and consequent muscle contraction, however without depending on neuronal



depolarization, that is, a direct effect on the muscle. Obviously, this hypothesis would greatly reduce the muscle fatigue factor resulting from the inhibition of nerve transmission in the myoneural plate caused by acidification in this region.

Petecchia et al.^[34] also demonstrate increased expression of voltage-dependent calcium channels in cultured cells. If the effect is reproducible in skeletal musculature, an avenue of possibilities opens for the effective gain in force generation and muscular efficiency, both in sports and aesthetics.

PEMF and postpartum abdominal diastasis

During pregnancy, the abdominal muscles are stretched and separated extensively to accommodate the growing fetus. However, the abdominal muscles often do not fully return to their original position and may remain separated after delivery. In severe cases, the separation of muscles can exceed 2.7 cm, characterizing a condition of abdominal diastasis. Jacob and Rank^[35] in a pilot study with 10 patients used the PEMF protocol twice a week for 30 minutes for 2 weeks. Patients were followed up 1, 3 and 6 months after the end of PEMF treatment.

Results obtained from magnetic resonance imaging showed an average fat reduction of 17% at one month and 20% after 3 months. The authors also reported a mean increase in muscle thickness of 20.5% after 1 month and 21.3% after 3 months. Especially, regarding the distance between the rectus abdominis muscles, a reduction of 16.7% in 01 month and 22.7% after 3 months. After six months, the authors report that 9 patients returned for evaluation, and showed, on average, a 17.6% fat reduction, a 21.7% increase in muscle, and a reduction in 23.2% of the distance between the abdominal muscles. The patients' weight did not change significantly. That study did not have a control group, but the initial results suggest a beneficial effect on fat reduction and muscle strengthening.

PEMF and Urinary Incontinence

Urinary incontinence (UI) is usually defined as the involuntary loss of urine. It is a chronic problem that negatively and significantly affects the quality of life^[36]. Urinary incontinence is classified as a) stress incontinence (SUI); b) urgent (IUU); c) Mixed (IUM).

The prevalence of urinary incontinence can vary between 25 and 45%, but can reach 69% in some populations, and the symptoms seem to worsen with advancing age, body mass index and some other factors^[37-61]. In general, the mechanism of urinary

incontinence is often associated with failure of the pelvic floor muscle apparatus.

Recently, Samuels et al.^[62] carried out a study with 75 patients with urinary incontinence and muscle strengthening using the PEMF technology. Of all 75 patients, 61 showed significant improvement of 49.93% of symptoms after 6 weeks of treatment and 64.4% after 3 months. The authors concluded that the PEMF technology was able to induce a significant improvement in the symptoms of urinary incontinence, especially mixed. In the 06-month follow-up after treatment, an improvement in the patients' quality of life was observed in relation to the problem.

On this same topic, Elena et al.^[63] investigated the efficiency of PEMF technology compared to classical electrical stimulation. The study was carried out with 95 women in the postpartum period who complained of urinary incontinence. Symptomatic patients received treatment with PEMF or electrostimulation in 10 sessions with a frequency of 2 to 3 times a week (PEMF – 28 minutes/session) or on alternate days (electrostimulation). In this study, 50 patients were treated with PEMF, 25 were treated with electrostimulation and 20 were considered as a healthy control group for comparison purposes. The authors report that the PEMF technology was able to significantly improve the biometric indices of pelvic floor integrity and symptoms of urinary incontinence, and that such results are due to the strengthening of the pelvic floor musculature. Interestingly, the patients also reported less discomfort with the use of PEMF, when compared to the electric current.

CONCLUSION

Pulsed electromagnetic fields (PEMF) present relevant clinical and experimental evidence of beneficial effects in the treatment of several musculoskeletal inflammatory disorders, such as tendinopathies and osteoarthritis, in addition to the treatment of urinary incontinence and abdominal diastasis. The evidence found goes beyond the described muscle-building effects. Placebo-controlled randomized clinical trials are needed to improve the power of evidence of current data. However, PEMF can be considered as the evolution of electrical currents for the treatment of musculoskeletal disorders, mainly due to its better tolerance by patients.

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Critical reviewer of the selected studies. Rodrigo Alvaro B. Lopes-Martins – General Coordinator and Chief of the Research Group.

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9.4 Anexo 4 - Evaluation of pulsed electromagnetic field therapy to improve muscle strength and functional aspects in the elderly: A pilot study



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Evaluation of pulsed electromagnetic field therapy to improve muscle strength and functional aspects in the elderly: A pilot study

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ABSTRACT

Background: Sarcopenia has been defined as a progressive and generalized disorder of skeletal muscle that involves accelerated loss of muscle mass and function. The prevalence of sarcopenia worldwide is up to 15% in healthy elderly, approximately 76% of acutely hospitalized elderly patients, and up to 69% of patients admitted for post-acute geriatric rehabilitation. The loss of muscle mass results in serious consequences and several chronic diseases and senility, characterized by functional losses, muscle weakness, loss of independence and increased risk of falls and death. Sarcopenia has been defined as a progressive and generalized muscle disorder. Here we investigate the effects of PEMF in muscle strength and functional capabilities of elderly sarcopenic patients. **Methods:** Fifteen elderly people of both sexes, aged between 65 and 80 years old, classified according to the degree of muscle weakness. The participants were submitted to PEMF therapy in 12 sessions three times a week with the following parameters. In the first two sessions, only submaximal contraction was applied during 30 min with a frequency of 5 Hz at the sport mode of the equipment. In the following 10 sessions we used cycles of Submaximal contractions – frequency of 5 Hz with 3s duration and Supramaximal contractions – frequency of 30 Hz with 3s duration. The intensity of the equipment was adjusted according to the sensitivity of the patient and session duration was 30 min. **Results:** The TUG functional tests showed a significant reduction in execution time, with an initial average of 40 ± 10s to 22 ± 6s after treatment sessions. The average increase in muscle strength was 27 ± 9% after PEMF treatment. **Conclusions:** This case series report is the first in the world scientific literature to demonstrate the effectiveness of PEMF (Supramaximus™) therapy in gaining muscle strength and functionality in elderly sarcopenic patients. PEMF therapy, at least for the treatment of sarcopenia in the elderly, can be considered as the definitive evolution of electrical currents, with greater effectiveness and acceptance by the patient. **Keywords:** Sarcopenia; Pulsed electromagnetic field; Aging; PEMF; Geriatrics.

BACKGROUND

The human being's remarkable ability to quickly adapt to constantly changing environmental and internal cues is vital to the health and survival of the organism. Most notable in human aging are changes in physiology and body composition, such as changes or redistribution in muscle and fat mass, even as total body weight remains unchanged^[1].

In Human Beings, muscle mass remains relatively stable during early life, but after the age of 30, a natural process of muscle mass reduction begins at a rate of 0.5 to 1.0% per year^[2]. With the aging process, the impaired balance between protein synthesis and proteolysis in skeletal muscle results in a progressive decline in skeletal muscle mass, strength and function and is defined as sarcopenia^[3]. As the strength of the limb muscles and respiratory muscles gradually decreases, normal physical functions and activities such as breathing, standing, walking, and running will also decrease^[3]. On average, peak strength decreases by 20-40% between ages 30 and 80. The loss of muscle mass results in serious consequences and various chronic diseases and senility, characterized by functional losses, muscle weakness, loss of independence and increased risk of falls and death^[4].

Sarcopenia has been defined as a progressive and generalized disorder of skeletal muscle that involves accelerated loss of muscle mass and function^[5]. In terms of human health, sarcopenia is associated with increased adverse outcomes including falls^[6], functional decline^[7], frailty and mortality^[8]. From a financial point of view, sarcopenia directly increases healthcare costs in society^[9,10]. The prevalence of sarcopenia worldwide is up to 15% in healthy elderly^[11], approximately 76% of acutely hospitalized elderly patients^[12-14], and up to 69% of patients admitted for post-acute geriatric rehabilitation^[15]. Thus, preventing or reversing sarcopenia is an important approach in healthy aging, both from an individual and societal point of view.

Widely accepted diagnostic criteria for sarcopenia require measurements of 3 components: muscle mass, muscle strength, and physical performance^[16,17]. Although the algorithm and testing tools have undergone some changes over the last decade, the main components remain the same. The components are not only applied for diagnosis and determination of severity, but also for monitoring the development of sarcopenia.

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To date, physical activity, with a focus on resistance (strength) training, is endorsed as a first-line therapy for managing sarcopenia⁽¹⁸⁾. Randomized controlled clinical studies have shown positive effects of resistance training on muscle mass, muscle strength and physical performance^(19,20). Such protocols remain as a reference standard for the prevention and treatment of sarcopenia in the elderly, but some technological innovations already available on the market such as the Pulsed Electromagnetic Field (PEMF) technology may represent an important advance for the situation.

Pulsed Electromagnetic Field (PEMF)

PEMF uses alternating magnetic fields, based on the law of electromagnetic induction, promotes electrical currents that depolarize the neuromuscular tissue, causing supramaximal contractions⁽²¹⁻²³⁾. Motor neurons are activated due to their large diameter and therefore lower resistance compared to other types of neurons. Since the nociceptors are not activated, the application of magnetic stimulation is not painful^(24,25).

PEMF and Muscle Hypertrophy

According to Duncan & Dinev⁽²⁶⁾, in an in vivo study carried out in a porcine experimental model, PEMF was able to induce hypertrophic muscle alterations after 2 weeks of treatment. The authors report an increase in muscle mass density of 20.56%. In the same study, an increase in muscle fiber density (hyperplasia) of 8.0% was observed. Mean individual muscle fiber size increased by 12.15% 2 weeks after treatment, while the control group showed no significant changes in fiber density or hyperplasia. The authors suggest that PEMF can be used for non-invasive induction of muscle growth. Pulsed Electromagnetic Field (PEMF) technology is an innovative technology that has shown important results in gaining strength and muscle mass. Here we performed a pilot study in order to investigate the concept that PEMF technology is capable of producing gains in muscle strength and functionality in the elderly, contributing to the prevention of sarcopenia.

METHODS

So far, 15 elderly people of both sexes, aged between 65 and 80 years old, classified according to the degree of muscle weakness, have been treated. The elderly attended underwent a standard elderly health anamnesis and received the standard treatment of muscle stretching, warm-up and PEMF training. Because it is a university extension project, there was no control

group and the inclusion and exclusion criteria were limited to cardiovascular diseases or some inability to move the lower limbs. The pulsed electromagnetic field generator Supramaximus™ (Adoxy Inc. Sorocaba – Brasil) was used in the study.

Clinical Anamnesis

Clinical evaluation: medical history and physical examination were performed. Vital Signs and Anthropometry included systolic and diastolic blood pressure in the sitting position, heart rate (pulse), axillary temperature in °C, height and weight measurements, and body mass index (BMI). Blood pressure was considered normal within the following limits: 90-139 mmHg for systolic and 50-89 mmHg for diastolic. Cardiac frequency within 50-100 bpm was considered normal. Participants with BMI in the range of 18 to 33 kg/m² were accepted.

Inclusion Criteria

Participants were accepted if they could be included in the following criteria: Male or female research participants aged 65 years or older and aged 80 years or less; Preserved cognitive capacity; No other significant illnesses that may impact their participation in the study, in accordance with the rules defined in the Protocol, and assessments; Cognitive function able to understand the nature and purpose of the study, including risks and adverse effects and with the intention to cooperate with the researcher and act in accordance with the requirements of the entire trial, which is confirmed by signing the Consent Form Free and Enlightened.

Exclusion Criteria

Participants were excluded if the present: Severe cardiovascular or cerebrovascular disease; Participant with current evidence of clinically significant diseases, of origin: gastrointestinal, cardiovascular, hepatic, renal, pulmonary, or other that prevent the individual's participation in the study and/or that, in the judgment of the main researcher, expose the research participant to additional risk than normally anticipated such as lupus erythematosus; Drug addiction, including alcohol; Performed any previous treatment for the lesion in question that, in the judgment of the main researcher, may interfere with the study objectives; BMI below 18 or above 33 kg/m²; The research participant has any condition that prevents him from participating in the study in the judgment of the investigator.



Assessment of gait, postural balance and functional mobility

Gait analysis was performed using the SMART-D 140® program (BTS Engineering, Milan, Italy) with a sampling rate of 100 Hz, eight cameras sensitive to the infrared spectrum and the SMART-D® (BTS Engineering, Milan, Italy) with 32 analog channels. All participants wore swimsuits to facilitate the placement of the reflective markers.

After the anthropometric measurements (height, weight, lower limb length, distance between the femoral condyles or diameter of the knee, distance between the malleoli or diameter of the ankle, distance between the anterior superior iliac spines or thickness of the pelvis and vertical distance on the sagittal plane in the supine position between the anterior superior iliac spine and great trochanter), passive markers were placed at specific reference points directly on the skin to evaluate the kinematics of each segment of the body, as described by Davis et al.⁽⁴⁵⁾ After placement of the reflective markers, the participants were instructed to walk along a 10-m track at comfortable pace. At least six trials were performed (two sets of three). For each participant, three out of the six trials that were consistent in terms of gait pattern were considered for analysis. All data were exported in .txt format to electronic spreadsheets and tabulated using Microsoft Office Excel® 2013 (Redmon, IL, USA).

The following were the spatiotemporal variables: velocity (m/s) (mean velocity of progression), step length (m, longitudinal distance between the point of initial contact of one foot and the point of initial contact of the contralateral foot), step width (m, distance between the rear end of the right and left heel centerlines along the mediolateral axis) stance phase (% gait cycle that begins with initial contact and ends with toe-off of the same limb) and double support (s, period of time when both feet are in contact with the ground).

The Six-Minute Walk Test (6 MWT) was performed to determine the degree of mobility and the speed to be used on the treadmill. This is a simple test developed to evaluate functional capacity through the measure of the distance traveled in a given period of time. Each volunteer was instructed to walk at a self-selected pace without running for six-minutes along a 30-m track. The volunteer was allowed to vary the pace and stop to rest, if necessary. The test was performed twice: once for familiarization and once to record the distance travelled, which was transformed from m/s to km/h to determine the treadmill training speed. A one-

week interval was respected between the first and second tests. Blood pressure and heart rate were monitored to ensure cardiovascular stability.

Assessment of functional mobility: Timed Up and Go Test (TUG)

The Timed Up and Go (TUG) test is widely used to assess functional mobility and dynamic functional balance. This test also quantifies, in seconds, the time that the individual performs the task, that is, in how many seconds he gets up from a standardized chair without support and arms, walks three meters, turns around, goes back to the chair and sits down again. Participants were instructed to perform the test at a self-selected speed in a safe manner.

Evaluation of Muscle Strength by Dynamometry

Muscle strength assessments of lower and upper limbs were performed with the E-elastic Computerized Dynamometry System. It is a dynamometer that can be attached to any part of the body, based on a load cell capable of evaluating the force produced by a muscle, as well as the speed and acceleration of the limb movement. The system is capable of transmitting data in real time to a cell phone or notebook via Bluetooth and even remotely via the internet to a central.

A series of 03 maximum contractions (triplicate) were performed for each evaluated member, being extension and flexion of the knee and trunk. The force value was taken into account the greatest force produced in the 3 attempts.

The system has a set of bracelets that adapt to the member, not causing any kind of discomfort or discomfort, except for the production of the participant's own strength.

Pulsed Electromagnetic Field Treatments

The participants were submitted to PEMF therapy in 12 sessions three times a week with the following parameters. In the first two sessions only submaximal contraction was applied during 30 min with a frequency of 5 Hz at the sport mode of the Supramaximus™ equipment. In the following 10 sessions we used cycles of Submaximal contractions – frequency of 5 Hz with 5s duration and Supramaximal contractions – frequency of 30 Hz with 5s duration. The intensity of the equipment was adjusted according to the sensitivity of the patient and session duration was 30 min.





RESULTS

Individual Muscle Force Increases

Figure 1A demonstrate the individual increases in muscle force quantified by the dynamometer system. Absolute values were used and as we can observe, all participants presented positive variations in muscle strength. Figure 1B shows the average and standard deviation of the group, concerning on muscle strength before and after pulsed electromagnetic therapy of the elderly participants.

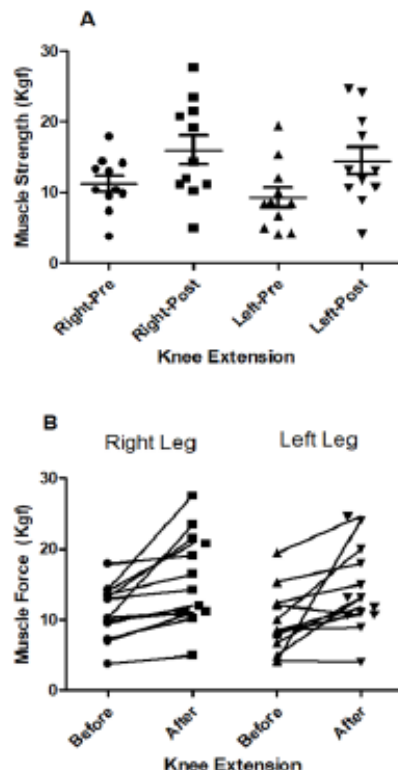


Figure 1. Individual values of Muscle force, before and after pulsed electromagnetic field therapy with Supramaximus in 13 elderly sarcopenic participants.

Differences (asymmetries) in Muscle Strength between Members

Figure 2 demonstrates the differences in muscle strength between the lower limbs of the treated elderly. We can observe that there were no significant differences regarding the differences in strength between the treated sides, before and after the electromagnetic field therapy. The average difference between limbs before treatment was approximately 2 Kg, and after treatment it was 1.8 Kg, demonstrating that the increase in muscle strength occurred linearly for both treated sides.

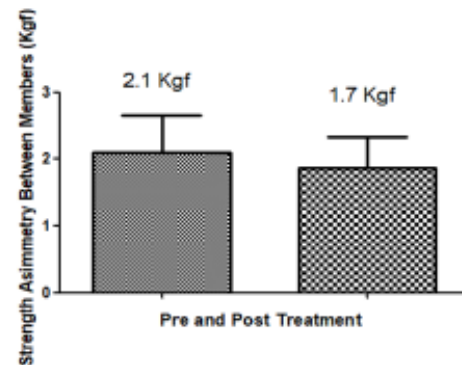


Figure 2. The graph quantitatively demonstrates the differences in muscle strength between the right and left limbs, before and after treatment with an electromagnetic field.

TUG test

As can be seen in Figure 3, the TUG functional tests showed a significant reduction in execution time, with an initial average of 40 ± 10 s to 22 ± 6 s after treatment sessions with pulsed electromagnetic field therapy (PEMF). of gait and balance demonstrated an average reduction of 47% after treatment with PEMF for 10 weeks.

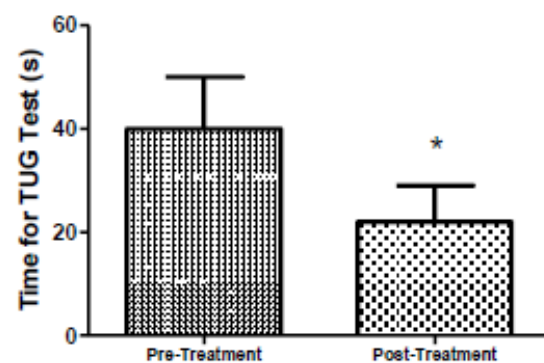


Figure 3. Shows the time values for performing the TUG Test (time up and go) which evaluates functionality in the elderly.

DISCUSSION

Several studies have shown that humans are unable to fully activate muscles voluntarily as the strength of muscles to contract is limited by the firing rates and conductivity of neural pathways⁽²⁷⁻²⁹⁾.

PEMF generates impulses that are independent of brain function, and with a frequency so fast that it does not allow for the muscle relaxation phase, characterizing tetanic contractions. To simulate muscle



workload conditions, the equipment modulates the PEMF emission in submaximal modes, from 1Hz to 10Hz and supramaximal mode, from 10Hz to 100Hz, with ON time in seconds that can also be parameterized (0 to 60s). In our study we combined both, low and high frequency stimulation and we were able to observe significant muscle strength after 12 sessions. The adopted protocol intended to provide an initial adaptation to the new sensations to the elderly patient. The training protocol adopted in this study was significantly efficient for gaining muscle strength in treated patients. As can be seen in figures 1A and 1B, all participants showed a positive result in strength increment after the 12 treatment sessions. A limitation of our study is that strength gain was not, at this time, compared with another type of intervention. A large study is currently being developed for comparison purposes.

PEMF has the ability to generate sustained supramaximal contractions for several seconds, which significantly increases stress/workload if muscle adaptation occurs^[30]. The recommended treatment for sarcopenia of the elderly is physical activity, especially focused on resistance muscle strengthening training. However, the methods used to date to gain strength and muscle mass focus on bodybuilding exercises or classic electrical currents. In both cases, we must consider the difficulties and physical, social and even sensitivity limitations of the elderly person, which ends up leading to low adherence to treatment and reduced chances of success. The resistance of elderly patients to attending gyms full of young people is well known, due to the natural constraints of older age in an environment that is not recognized as their own. In addition, most traditional fitness and weight training centers do not have the more personalized follow-up required by an elderly person with sarcopenia. On the other hand, there are the classic electric currents, used in physiotherapy, for muscle strengthening. In this case, the elderly patient is faced with another type of limitation, now related to sensitivity. The elderly patient, notably, presents increased sensitivity to painful stimuli, or even electrical currents, making the treatment unbearable. Data from our research group (unpublished) show that the degree of pain or hypersensitivity induced by electrical currents in elderly patients treated with this type of therapy, on a visual analogue scale (0 to 10), reaches values between 7 and 9. In the treatment with pulsed electromagnetic field, using the same scale, the degree of hypersensitivity or even pain did not exceed level 03, demonstrating a significantly greater adaptation or acceptance of therapy with pulsed electromagnetic field.

The results obtained in the functional tests also revealed a significant improvement, both in the execution time of the tasks and in the resourcefulness to carry them out. The improvement in muscle strength is directly related to the reduction of imbalances and falls in the elderly.

A second important point observed in Figure 03 was the reduction of muscle asymmetry in terms of strength. Before treatment, important asymmetries between limbs were observed, of the order of 2.1 kgf. Such asymmetries were reduced to 1.7 Kg on average, representing an improvement of 20%. It is important to point out that such a reduction in muscle asymmetries was obtained with standard treatment, equally applied to both limbs, that is, no specific protocol was performed to strengthen a weaker limb.

CONCLUSION

This case series report is the first in the world scientific literature to demonstrate the effectiveness of PEMF (Supramaximus®) therapy in gaining muscle strength and functionality in elderly sarcopenic patients. PEMF therapy, at least for the treatment of sarcopenia in the elderly, can be considered as an important alternative to electrical currents, with greater effectiveness and acceptance by the patient.

Authors Contribution: Patricia Sardinha Leonardo, Rodrigo Alvaro B. Lopes-Martins and Claudia Santos Oliveira – team leaders of the study; Katiele Rodrigues da Silva Cardoso, Bruno Oliveira Silva, Ruan Oliveira Silva, Helen Cristina de Araújo Silva, Paulo Ricardo Pinheiro França, Beatriz Nascimento Souza, Isabela Laine, Carly de Faria – Protocol and tests execution. Alberto Souza de Sá Filho – Critical Reading of the manuscript;

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