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FACULDADE DE MEDICINA

PROGRAMA DE PÓS-GRADUAÇÃO EM MEDICINA: CIÊNCIAS MÉDICAS

Dissertação de Mestrado

Sarcopenia em pacientes com Lúpus Eritematoso Sistêmico: Um estudo transversal

Émerson Pena

Porto Alegre

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Sarcopenia em pacientes com Lúpus Eritematoso Sistêmico: Um estudo transversal

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RESUMO

Base teórica: O lúpus eritematoso sistêmico (LES) é uma doença autoimune inflamatória crônica com envolvimento multissistêmico. Diversos órgãos e sistemas podem ser afetados, como o sistema musculo esquelético. Essa condição inflamatória pode levar à diminuição da força e da massa muscular e, consequentemente, à sarcopenia. A sarcopenia é considerada uma doença muscular que pode resultar na diminuição da funcionalidade física do paciente, no qual resulta também o aumento de riscos de quedas, fraturas, hospitalização e mortalidade. Apesar de ser um achado clínico relevante, a sarcopenia ainda é um assunto pouco estudado no LES.

Objetivo: (1) Realizar uma revisão sistemática com meta-análise para verificar a força muscular, massa muscular e performance física em pacientes com LES (artigo 1), (2) avaliar a prevalência de sarcopenia de acordo com diferentes critérios de classificação diagnóstica (EWGSOP2) (artigo 2), (3) verificar qual desses critérios de classificação diagnóstica é mais sensível e específico para pacientes com dano cumulativo do LES (artigo 2) e (4) avaliar a relação entre a prevalência de sarcopenia e parâmetros clínicos (artigo 2).

Métodos: Foi realizado uma revisão sistemática com meta-análise de estudos observacionais (artigo 1). Esta revisão incluiu artigos com dados de força muscular, massa muscular e performance física de pacientes com LES. A seguir, ainda com o objetivo de avaliar a prevalência de sarcopenia no LES, foi proposto um estudo transversal. Foram incluídas mulheres com LES (18 a 50 anos) e os seguintes dados foram coletados: tempo de doença, índice de dano (SLICC/ACR-DI), atividade da doença (SLEDAI-2k), tratamento farmacológico, qualidade de vida (SLEQoL), nível de atividade física (IPAQ) e força muscular. A massa muscular foi mensurada através do exame de Absorciometria por raios-X com dupla energia. Além disso, avaliamos por 3 parâmetros distintos, sendo massa muscular apendicular esquelética (ASM), ASM/altura² (ASMI) e ASM/Índice de massa muscular (IMC). A função física foi avaliada através do teste *timed up and go* (TUG) e da bateria curta de performance física (SPPB). Foram realizadas análises descritivas, coeficientes de correlação de Pearson ou Spearman, análise de sensibilidade e teste qui-quadrado. Considerou-se significância estatística $p<0,05$.

Resultados: Na revisão sistemática com meta-análise, foram encontrados 607 artigos completos. Após a revisão detalhada dos artigos, 19 artigos foram incluídos no nosso estudo e 11 artigos foram incluídos na meta-análise. Os principais achados desta revisão sistemática com meta-análise foram que pacientes com LES parecem ter menos força muscular avaliada pela preensão manual do que controles saudáveis (LES=21,74 kg; controles saudáveis=29,34 kg; $p<0,05$). Pacientes com LES parecem ter maior força que paciente com artrite reumatoide (AR), mas essa diferença não foi estatisticamente significativa (AR=17,24 kg; $p=0,210$). Pacientes com LES com artropatia deformante apresentam menor força muscular do que pacientes com LES sem artropatia deformante ($p<0,01$). A massa muscular foi semelhante nos pacientes com LES em relação ao grupo AR e controles ($p>0,05$). A função física parece estar regular nos pacientes com LES. No estudo transversal, foram incluídas 49 pacientes com idade de 35,0 (28,0–43,5) anos e tempo de doença de 8,0 (4,0–14,5) anos. A cronicidade e atividade da doença estavam baixas, 0,0 (0,0–1,0) e 2,0 (0,0–4,0), respectivamente. Doze pacientes estavam em uso de corticoides nos últimos 12 meses e a dose cumulativa foi de 2,73 (1,18–6,63) gramas. A prevalência de sarcopenia foi de 16,3% seguindo os critérios de classificação diagnóstica EWGSOP2 (teste de levantar-se da cadeira e ASM). Os pacientes apresentaram força muscular avaliada pelo teste de pressão palmar de 24,71±9,01 kg. Quando avaliada pelo teste de levantar-se da cadeira, a força muscular foi de 14,32±3,68 segundos. Os pacientes tiveram massa muscular avaliada pelo ASM de 17,03±2,32 kg, pelo ASMI de 6,70±0,88 kg/m² e pelo ASM/IMC de 0,63±0,11 kg. A função física se mostrou preservada nesses pacientes. Além disso, o diagnóstico de sarcopenia avaliado pelo teste de levantar-se da cadeira e ASM apresentou maior sensibilidade (28%) para pacientes com dano cumulativo da doença (SLICC/ACR-DI >0). Por fim, não houve associação entre sarcopenia e idade, duração da doença, cronicidade da doença, atividade da doença, dose cumulativa de corticosteroide, qualidade de vida e nível de atividade física ($p>0,05$).

Conclusão: A força muscular está alterada em pacientes com LES e pacientes com LES com artropatias deformantes têm menos força muscular do que pacientes sem artropatias deformantes. Em nosso estudo transversal a prevalência de sarcopenia foi de 16,3% em pacientes com LES. O diagnóstico de sarcopenia avaliado pelo teste de sentar e levantar e ASM demonstrou ser mais sensível (28%) para pacientes com dano cumulativo da doença. Entretanto, não foi encontrada associação de parâmetros clínicos com sarcopenia. Portanto, estudos longitudinais devem ser desenvolvidos para avaliar os fatores de risco para sarcopenia em pacientes com LES.

Palavras-chave: Lúpus eritematoso sistêmico, sarcopenia, força muscular, massa muscular, performance física.

ABSTRACT

Background: Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease with multisystem involvement. Organs and systems can be affected, such as the musculoskeletal system. This inflammatory condition can lead to decreased strength and muscle mass and, consequently, sarcopenia. Sarcopenia is considered a muscle disease that can result in decreased physical functionality of the patient, increased risk of falls, fractures, hospitalization and mortality. Despite being a relevant clinical finding, sarcopenia is still a little studied subject in SLE.

Objective: (1) To assess muscle strength, muscle mass and physical performance in patients with SLE, (2) to evaluate the prevalence of sarcopenia according to different diagnostic classification criteria (EWGSOP2), (3) to verify which classification criteria are more sensitive and specific for patients with cumulative damage from SLE and (4) to assess the relationship between the prevalence of sarcopenia and clinical parameters.

Methods: In order to verify the prevalence of sarcopenia in SLE patients in the literature, we performed a systematic review with meta-analysis of observational studies. As information on this subject is scarce, our review work included articles with data on muscle strength, muscle mass and physical performance of patients with SLE. In addition, with the aim of evaluating the prevalence of sarcopenia in SLE, a cross-sectional study was proposed. In this cross-sectional study, women with SLE (18 to 50 years old) were included. The following data were collected: Disease duration, damage index (SLICC/ACR-DI), disease activity (SLEDAI-2k), treatment regimen, quality of life (SLEQoL), physical activity level (IPAQ), muscle strength, muscle mass by dual-energy radiological absorptiometry (DXA). Muscle mass was evaluated by 3 different parameters (appendicular skeletal muscle mass (ASM), ASM/height^2 and ASM/BMI. Physical performance was evaluated by the Timed-up-and-go (TUG) and Short Physical Performance Battery (SPPB) test. The descriptive analysis, Pearson's or Spearman's correlation coefficients,

Sensibility analysis and Chi-squared test were performed. The significance was considered $p<0.05$.

Results: Nineteen studies were included in the systematic review and 11 articles were included in the meta-analysis. SLE patients appear to have less muscle strength assessed by handgrip than healthy controls (SLE=21.74 kg; healthy controls=29.34 kg; $p<0.05$). SLE patients seem to have greater strength then rheumatoid arthritis (RA), but this difference was not statistically significant (AR=17.24kg; $p=0.210$). However, in the sensitivity analysis, SLE group without deforming arthropathy showed higher muscle strength than the RA group ($p=0.0001$). SLE patients with deforming arthropathy have lower muscle strength than SLE patients without deforming arthropathy ($p<0.01$). Muscle mass was similar in SLE patients compared to the RA group and controls ($p>0.05$). In our cross-sectional study, forty-nine patients were included (Median age:35.00 (28.00–43.50) years; Median disease duration: 8.00 (4.00–14.50) years. Chronicity and disease activity were low, 0.0 (0.0–1.0) e 2.0 (0.0–4.0), respectively. Twelve patients were on glucocorticoid treatment in the last 12 months, with a median cumulative dose of 2.73 (1.18–6.63) grams. The prevalence of sarcopenia was 16.3% following the European Working Group on Sarcopenia in Older People-2 (EWGSOP2) criteria (chair stand test and ASM).

The patients presented muscle strength by the handgrip test of 24.71±9.01 kg and 14.32±3.68 seconds using the chair stand test. The patients had muscle mass assessed by the ASM of 17.03±2.32 kg, ASMI 6.70±0.88 kg and ASM/BMI 0.63±0.11 kg. Physical performance was preserved in these patients. In addition, the diagnosis of sarcopenia assessed by the chair-rising test and ASM showed higher sensitivity (28%) for patients with cumulative damage from the disease (SLICC/ACR-DI <0). Lastly, there was no association between sarcopenia and age, disease duration, disease chronicity, disease activity, cumulative corticosteroid dose, quality of life, and physical activity level ($p>0.05$).

Conclusion: Muscle strength is altered in SLE patients and SLE patients with deforming arthropathies have less muscle strength than patients without deforming arthropathies. In our cross-sectional study, the prevalence of sarcopenia was 16.3% in patients with SLE. The diagnosis of sarcopenia

assessed by the chair stand test and ASM demonstrated to be more sensitive (28%) for patients with cumulative disease damage. In contrast, no association of clinical parameters with sarcopenia was found. Therefore, longitudinal studies should be developed to assess risk factors for sarcopenia in patients with SLE.

Keywords: Systemic lupus erythematosus, sarcopenia, muscle strength, muscle mass, physical performance.

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LISTA DE ABREVIATURAS E SIGLAS

Sigla ou abreviação	Nomenclatura
ACR	Colégio americano de reumatologia *(American College of Rheumatology).*
AR	Artrite reumatoide.
ASM	Massa muscular esquelética apendicular *(Appendicular skeletal muscle mass)*.
ASMI	Índice de massa muscular esquelética apendicular *(Appendicular skeletal muscle mass index)*.
BIA	Bioimpedância elétrica.
DMO	Densidade mineral óssea.
DXA	Absorciometria por raios-X com dupla energia (dual-energy radiological absorptiometry).
EWGSOP	Grupo de trabalho europeu sobre sarcopenia em pessoas idosas.
FSS	Escalada de gravidade da fadiga *(fatigue severity scale).*
LES	Lúpus eritematoso sistêmico.
SF-36	Formulário de avaliação de qualidade de vida *(Short-form-36).*
VLA	Atividade de vida diária *(Valued life activities).*
SLICC	Colaboradores clínicos internacionais de lupus *(Systemic lupus international collaborating clinics).*
SPPB	Bateria de performance física curta *(short-physical performance battery).*
TUG	Tempo para levantar-se da cadeira e ir *(Timed up and go).*

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INTRODUÇÃO

O lúpus eritematoso sistêmico (LES) é uma doença autoimune inflamatória crônica com envolvimento multissistêmico [1,2]. A etiologia da doença é pouco conhecida, porém sabe-se da participação de fatores hormonais, ambientais, genéticos e imunológicos [3,4].

O LES pode afetar vários órgãos e sistemas, incluindo o sistema musculoesquelético [1,2,5] . Esse quadro inflamatório sistêmico pode influenciar na diminuição da massa muscular e da força muscular, levando consequentemente, a sarcopenia [6]. A sarcopenia é considerada uma doença muscular (falha muscular) caracterizada pela redução da força muscular e massa muscular [7]. Essa doença pode levar os indivíduos a uma diminuição da funcionalidade física, resultando no aumento de riscos de quedas, fraturas, hospitalização e mortalidade [8].

Até o presente momento há uma escassez de estudos que avaliaram a sarcopenia no LES. Santos e colaboradores (2011) utilizaram o critério de diagnóstico para definir sarcopenia com índice de massa livre de gordura ≤2 desvios-padrão (DP) abaixo da média de uma população caucasiana de referência [9] . Neste estudo, 92 mulheres com LES foram avaliadas e a prevalência de sarcopenia foi de 10,9%.

Assim, algumas perguntas necessitam ser investigadas: Qual a prevalência de sarcopenia em paciente com LES? A função física é reduzida em pacientes com LES? Qual a diferença da força muscular e massa muscular entre pacientes com LES quando comparados a grupo controle? Quais são os fatores associados à sarcopenia em pacientes com LES?

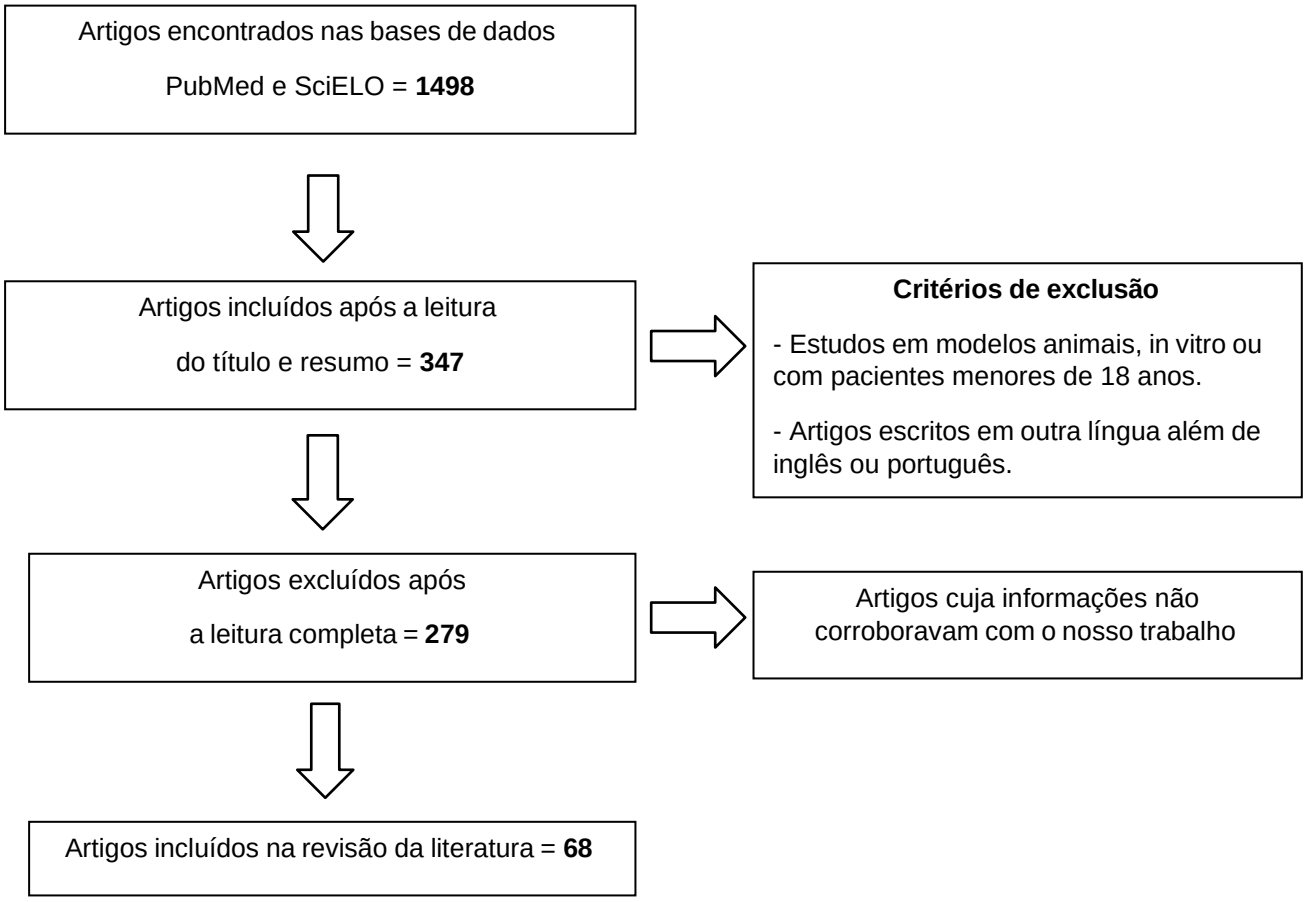
Esta dissertação segue a disposição de: uma revisão da literatura (para apresentação do referencial teórico que deu base ao trabalho), um artigo de revisão sistemática com meta-análise [artigo um (1) da dissertação] e um artigo original que apresenta os dados do estudo transversal que avaliou a sarcopenia em pacientes com LES [artigo dois (2) da dissertação].

REVISÃO DA LITERATURA

2.1 Estratégias para localizar e selecionar informações

Para esta revisão da literatura, o objetivo foi buscar aspectos relacionados a sarcopenia e ao LES, bem como combinações e MeSH termos ligados a essas doenças. A estratégia de busca envolveu bases de dados como: PubMed e SciELO (publicados até novembro de 2022). As palavras-usadas foram: *Systemic Lupus Erythematosus*, *Pathogenesis*, *Diagnosis criteria* e *Sarcopenia*.

Figura 1. Estratégia de busca e seleção dos artigos.



2.2 Lúpus eritematoso sistêmico

O lúpus eritematoso sistêmico (LES) é uma doença autoimune, inflamatória, crônica, e com envolvimento multissistêmico. Suas manifestações podem ocorrer nos rins (nefrite lúpica), sistemas digestório, pulmonar e cardiovascular, no sistema nervoso central (lúpus neuropsiquiátrico), na pele (lesões mucocutâneas), no sangue, entre outros [2,5,10]. Além disso, pacientes com LES também podem desenvolver manifestações no sistema musculoesquelético e articular (artrite e miosite), com diminuição da força muscular, massa muscular e função física [5,11].

2.3 Epidemiologia

Na população mundial a prevalência de LES é de 241/100.000 e a incidência varia entre 0,3/100.000 e 23,2/100.000 ao ano [12–16]. Na população brasileira, a taxa de incidência de 8,7 por 100.000/ano [16]. Além disso, o LES atinge mais mulheres do que homens, sendo uma proporção de 2:1 até 15:1, dependendo do país e da faixa etária acometida [15].

2.4 Patogênese do LES

O LES é caracterizado por uma quebra na homeostase imunológica, embora o mecanismo que desencadeie a patogenia do LES ainda seja pouco elucidado. Sabe-se que ativação anormal de células T e B é responsável por essa quebra de tolerância imune [3,17–19].

Um mecanismo mais bem compreendido na literatura sobre a patogênese do LES seria o desequilíbrio entre a apoptose e a depuração deste material apoptótico. Os *debris* apoptóticos, em geral, são retirados rapidamente do organismo e não são acessíveis ao sistema imune. Entretanto, quando há falhas e permanência de alguns *debris* contendo ácidos nucleicos, pode-se estimular uma resposta imunomediada através da ativação de receptores de reconhecimento de ácidos nucléicos como, por exemplo, os receptores do tipo Toll (TLR) [20].

Outro processo que pode contribuir para a patogênese da doença seria a disfunção de células dendríticas e neutrófilos. Estas células seriam responsáveis pela expansão de células T autorreativas e células B com produção de autoanticorpos patogênicos e citocinas inflamatórias [21,22]. Existe também uma

correlação entre o LES e o anticorpo C1q, onde evidências apontam que a deficiência de C1q pode inibir a eliminação de células apoptóticas, podendo aumentar a exposição a autoantígenos e contribuir no processo inflamatório [23,24].

Além disso, fatores hormonais, ambientais, imunológicos e, principalmente, genéticos estão envolvidos na etiologia da doença [3,4]. Alguns desses fatores apresentam dados conflitantes quanto a possível etiologia do LES em pacientes, como: exposição a radiações, metais pesados, solventes e pesticidas, infecções, vacinas e fatores dietéticos [25,26]. Outros fatores são mais elucidados na literatura, como o tabagismo, exposição a sílica, anticoncepcionais orais, terapias hormonais pós-menopausa e a hereditariedade [25] . A predisposição genética tem um papel determinante na suscetibilidade dos pacientes, parentes de primeiro grau são 17 vezes mais suscetíveis a desenvolverem LES do que a população geral [27]. Os fatores ambientais podem causar alterações epigenéticas, que pode desencadear ou acelerar o surgimento da doença [28].

2.5 Classificação diagnóstica do LES

Em 1982 o colégio americano de reumatologia (American College of Rheumatology – ACR) estabeleceu 11 critérios para a classificação diagnóstica do LES, que foram revisados em 1997 [29]. Em 2012, o grupo internacional de pesquisa clínica do LES (SLICC) gerou um documento com algumas modificações, a fim de aumentar a sensibilidade e permitir o diagnóstico precoce do LES [30]. Estes critérios de classificação diagnóstica (SLICC-2012) foram baseados em achados clínicos e imunológicos, onde o paciente deveria pontuar 4 ou mais itens, sendo no mínimo 1 critério clínico e 1 critério imunológico [30]. Os critérios de classificação SLICC-2012 demonstraram ter uma sensibilidade maior, mas uma especificidade menor, quando comparados aos critérios do ACR-1997.

Em 2019, membros do EULAR e ACR propuseram em conjunto uma atualização dos critérios de classificação diagnóstica, a fim de melhorarem a sensibilidade e a especificidade desta ferramenta [31] . Nesta atualização, os anticorpos antinucleares (ANA) positivos foram considerados um critério de entrada obrigatório, seguido de critérios clínicos e imunológicos. Os critérios

variam entre 2 e 10 pontos em diferentes domínios e pacientes com ≥10 pontos são classificados com diagnóstico de LES [31]. Este consenso teve êxito no seu objetivo de conciliar a alta especificidade dos critérios do ACR-1997 com a alta sensibilidade dos critérios SLICC-2012 e vem sendo muito utilizado em estudos clínicos.

2.6 Manifestações articulares e extra articulares no LES

Sabe-se que os pacientes com LES podem desenvolver muitas manifestações articulares e extra-articulares.

2.6.1 Articulações

O envolvimento musculoesquelético é comumente observado em pacientes com LES [32–35]. Cornet e colaboradores (2020), avaliaram mais de 4 mil mulheres e as manifestações clínicas encontradas com maior prevalência: articulações (81,8%), pele (59,4%) e músculos (41,6%) [35] . Cervera e colaboradores (2013), realizaram um estudo multicêntrico composto por 373 mulheres e 39 homens com LES e observaram que os 5 sistemas mais afetados cronicamente foram: musculoesquelético (14,3%), neuropsiquiátrico (12,9%), renal (7,5%), ocular (7,5%) e cutâneo (6,8%) [36].

Dentre as manifestações articulares, a artralgia e a artrite apresentam alta prevalência, podendo chegar a 84% em pacientes com LES [37]. As erosões articulares apresentam uma menor prevalência, variando de 30 a 47%, dependendo da técnica de imagem utilizada para avaliação [38–40]. Outra manifestação articular observada no LES é a artropatia deformante conhecida como artropatia de Jaccoud [41–43]. Essa manifestação afeta cerca de 5% dos pacientes com LES [44,45]. A osteonecrose é outra manifestação articular observada em pacientes com LES. Sua prevalência pode variar de 4 a 15% e as principais articulações atingidas são os joelhos e as articulações coxofemorais [46–48].

Além dessas manifestações articulares, pacientes com LES podem apresentar manifestações extra articulares, como fadiga, baixa força e redução da massa muscular e da função física.

2.6.2 Fadiga

A fadiga é um sintoma extra articular comumente relatado pelos pacientes com LES. Sua prevalência pode variar entre 80 e 90% [35,49–51]**.** Uma parcela importante de pacientes (45,5%) relata que a fadiga interfere em seu funcionamento físico e 55,1% de pacientes com LES gostariam que esse sintoma "desaparecesse" [35,51]. Este sintoma apresenta associação negativa com a qualidade de vida, com a atividade de vida diária (ATVD) e com a força muscular de pacientes com LES [52–54].

2.6.3 Força muscular

A força muscular é uma capacidade física importante para execução das ATVD. A diminuição da força muscular pode levar a um prejuízo na função física, interferindo na realização das ATVD e na qualidade de vida dos pacientes.

Balsamo e colaboradores (2013), avaliaram força de preensão palmar e força dinâmica dos pacientes com LES e indivíduos saudáveis (grupo controle) [54]. Foram realizados exercícios de *leg press, chest press, leg extension, lat pulldown e leg curl* (pressão de pernas, pressão de peito, extensão de pernas, puxada para baixo e flexão de perna). Os pacientes com LES apresentaram menor força muscular em ambos os testes quando comparados ao grupo controle ($p<0,05$). A baixa força muscular também se associou negativamente com a fadiga, desempenho funcional e qualidade de vida [54] . Corroborando com esses achados, Andrews e colaboradores (2015), avaliaram 146 mulheres adultas com LES e demonstraram que a redução da força muscular dos membros inferiores associou-se também ao aumento da deficiência física autorreferida e incapacidade física [55].

Em uma revisão sistemática com meta-análise foi verificado que pacientes com LES apresentam uma força muscular (teste de preensão palmar) menor quando comparados a indivíduos saudáveis (artigo 1 desta dissertação). Além disso, foi verificado que pacientes com LES apresentam maior força muscular (21,74 kg), quando comparados com pacientes com artrite reumatoide (AR) (17,24 kg). Entretanto, dois outros estudos avaliaram a força muscular em pacientes com LES e com artropatias deformantes (artropatia de Jaccoud, artropatia deformante leve e artrite erosiva) e demonstraram uma semelhança entre os valores de força de pacientes com LES e artropatia deformante, quando

comparados a pacientes com AR [42,43]. Ainda, quando comparamos pacientes com LES sem artropatia deformante e pacientes com LES com artropatia deformante, os pacientes com artropatia deformante apresentaram menor força muscular, quando avaliados pelo teste de preensão palmar.

2.6.4 Massa muscular

A massa muscular é um conjunto formado pelos músculos, sendo essencial para estrutura corporal. Revisão sistemática com meta-análise encontrou 5 artigos que avaliaram a massa magra (kg) de pacientes com LES e compararam com indivíduos saudáveis [9,54,56–58]. Não foi encontrada diferença estatisticamente significativa entre os grupos LES e controles ($p>0,05$). Um estudo também comparou a massa livre de gordura entre pacientes com LES, AR e indivíduos saudáveis [9] .Também não foi encontrado diferença entre os grupos em relação a massa livre de gordura.

Dois estudos inseridos na revisão sistemática ajustaram a massa esquelética apendicular dividida pela altura² (ASM/altura²), utilizando então o valor de índice de massa muscular (ASMI) [59,60]. Os valores encontrados em ambos os artigos foram semelhantes quanto a ASMI, sendo 6,97 kg e 6,1±1,1 kg, respectivamente [59,60]. Outro estudo ajustou o índice de massa magra dividido pelo índice da massa gorda [55]. O valor encontrado foi de 1,7±0,6 kg. Apesar de serem encontrados estudos com diferentes métodos de ajustes de massa muscular, todos estes ajustes são cientificamente validados [6].

Quanto a fatores associados com alterações de massa muscular no LES, apenas um estudo avaliou a influência do uso de glicocorticoide na massa muscular. Mok e colaboradores (2008), verificaram que a administração de corticoide, durante (2 meses) e após (6 meses) não altera a massa magra de pacientes com LES ($p>0,05$) [61] . Portanto, mais estudos são necessários para elucidar os fatores associados às alterações de massa muscular no LES.

2.6.5 Função física

A função física é um componente que pode ser afetado pelas alterações de força muscular e massa muscular. Existem poucos estudos que avaliaram a função física de pacientes com LES com testes objetivos. Dois estudos [62,63] mensuraram a função física através *short physical performance battery* (SPPB)

e um estudo [54] avaliou a função física através do teste de *timed up and go* (TUG).

Andrews e colaboradores (2015), avaliaram 105 mulheres com LES com idade de 47,8±12,3 anos e duração da doença de 15,5±9,2 anos. O valor do teste SPPB foi de 10,2±1,9 pontos, demonstrando que estes 105 pacientes com LES apresentaram boa função física [63]. Corroborando com Andrews e colaboradores (2015), Plantinga e colaboradores (2018), avaliaram 60 pacientes (90% mulheres) com idade média de 47,9±12,6 anos e duração da doença de 17,7±10,9 anos [62]. Os pacientes apresentaram 8,8 pontos no SPPB, demonstrando também uma boa função física. A função física avaliada pelo teste de TUG foi utilizado em apenas 1 estudo com pacientes com LES [54]. Balsamo e colaboradores (2013), avaliaram 25 mulheres em acompanhamento no ambulatório de reumatologia do Hospital Universitário de Brasília (Brasil) e 25 mulheres saudáveis pareadas por idade, IMC, massa corporal magra e massa gorda. O grupo LES apresentava idade de 29,9 (6,8) anos, duração da doença de 5,3±4,6 anos e baixa atividade da doença 1,5±1,2 medida pelo SLEDAI. O tempo encontrado para realização do TUG no grupo de pacientes com LES e do grupo controle foi de 5,3±0,4 e 5,0±0,6 segundos, respectivamente, demonstrando que ambos os grupos apresentaram boa função física avaliada pelo TUG.

Portanto, os estudos que avaliaram função física medidos de forma objetiva demonstram que os pacientes com LES apresentam função física regular. Porém, ainda são poucos estudos que avaliaram este desfecho. Assim, é necessário que a função física seja mais explorada em estudos com LES.

2.7 Sarcopenia

A sarcopenia é considerada uma doença caracterizada pela redução da força muscular e massa muscular [6,7]. Como consequência, a sarcopenia pode acarretar dependências funcionais, aumento do risco de quedas, fraturas, hospitalização e mortalidade [8,64–66].

Os mecanismos envolvidos tanto no aparecimento como na progressão da sarcopenia são: idade, desuso, nutrição inadequada, caquexia, doenças neurodegenerativas e fatores endócrinos [7].

2.7.1 Diagnóstico de sarcopenia

Existem diversos grupos de trabalho em sarcopenia que apresentam critérios de diagnóstico. O diagnóstico de sarcopenia é realizado a partir da avaliação da força muscular e massa muscular. Para avaliar a gravidade da sarcopenia, é realizada a avaliação da performance física do paciente (tabela 1). As medidas e pontos de corte para sarcopenia de cada grupo está sumarizado na tabela 2.

Tabela 1. Ferramentas para avaliar a sarcopenia.

Força muscular	Massa muscular	Performance física
	Quantidade muscular	
Preensão palmar	DXA	5 Repetições - teste da cadeira
Suporte de cadeira	CT	SPPB
	MRI	6 metros de caminhada
	BIA	400 metros de caminhada
	Antropometria	Velocidade de caminhada
	Qualidade muscular	TUG
	Teste de diluição de creatina	
	Ultrassonografia	
	Biomarcadores específicos ou painéis de biomarcadores	

Abreviações: DXA= Absorciometria por raios-X com dupla energia; CT= Tomografia computadorizada; MRI= Ressonância magnética por imagem; BIA= Bioimpedância elétrica; SPPB= Bateria de performance física curta; TUG= Tempo para levantar-se da cadeira e ir.

Tabela 2. Pontos de corte para sarcopenia.

		Instrumento	Ponto de corte
Força muscular			
Força de preensão			
	EWGSOP2	Dinamômetro Jamar	<27kg para homem <16kg para mulher
	FNIH		GSMAX <26kg para homem <16kg para mulher
			$GSMAX_{IMC}$ <1 para homem <0,56 para mulher
	AWGS		<28kg para homem <18kg para mulher

	Baker et al.	-	-
Suporte de cadeira			
	EWGSOP2	Cadeira	>15s para 5 subidas
	FNIH	-	-
	AWGS	-	-
	Baker et al.	-	-
Massa muscular			
ASM			
	EWGSOP2	DXA BIA CT MRI	<20kg para homem <15kg para mulher
	FNIH	-	-
	AWGS	DXA BIA	<7,0kg/m² para homem <5,4kg/m² para mulher <7,0kg/m² para homem <5,7kg/m² para mulher
	Baker et al.	-	-
ASMI			
	EWGSOP2	DXA BIA CT MRI	<7,0kg/m2 para homem <5,5kg/m2 para mulher
	FNIH	-	-
	AWGS	-	-
	Baker et al.	-	-
ALM			
	EWGSOP2	-	-
	FNIH	DXA	<19,75 kg para homem <15,02kg para mulher
	AWGS	-	-
	Baker et al.	-	-
ALM_{BMI}			
	EWGSOP2	-	-
	FNIH	DXA	<0,789 para homem <0,512 para mulher
	AWGS	-	-

	Baker et al.	-	-
$ALMI_{FMI}$		-	-
	EWGSOP2	-	-
	FNIH	-	-
	AWGS	-	-
	Baker et al.	DXA	< 2,0 Z score
Performance física			
	EWGSOP2	Velocidade da marcha	≤0,8 m/s
		SPPB	≤8 pontuações score
		TUG	≥20 s
		400 m teste de caminhada	Incompleto ou ≥6 minutes para completar
	FNIH	-	-
	AWGS	6 Metros de caminhada	<1,0m/s
		5 Repetições - teste da cadeira	≥12 s
		SPPB	≤ 9
	Baker et al.	-	-

Abreviações: EWGSOP2= Grupo de trabalho europeu sobre sarcopenia em pessoas idosas; FNIH= Fundação para os institutos nacionais de saúde; AWGS= Grupo de trabalho asiático para sarcopenia; ASM=Massa magra esquelética apendicular; ASMI= Massa magra apendicular ajustada para altura²; ALM= Massa magra apendicular; ALM_{imc}= Massa magra apendicular ajustada para o índice de massa corporal; $ALMI_{FM}$= Massa magra apendicular ajustada para o índice de massa gorda; DXA= Absorciometria por raios-X com dupla energia; CT= Tomografia computadorizada; MRI= Ressonância magnética por imagem; BIA= Bioimpedância elétrica; SPPB= Bateria de performance física curta; TUG= Tempo para levantar-se da cadeira e ir.

2.7.2 Sarcopenia no LES

Dados sobre a prevalência de sarcopenia no LES são escassos. Santos e colaboradores (2011), estimaram a prevalência de sarcopenia através do exame de bioimpedância elétrica e utilizaram como critério de diagnóstico apenas o índice de baixa massa magra dividido pela altura². Mulheres com valores ≤13,4 kg, foram consideradas sarcopênicas [9,67]. A prevalência de sarcopenia encontrada em pacientes com LES foi de 10,9%. Além disso, este

estudo demonstrou que existe uma maior probabilidade de pacientes com LES desenvolverem sarcopenia, quando comparados a pacientes com AR [9].

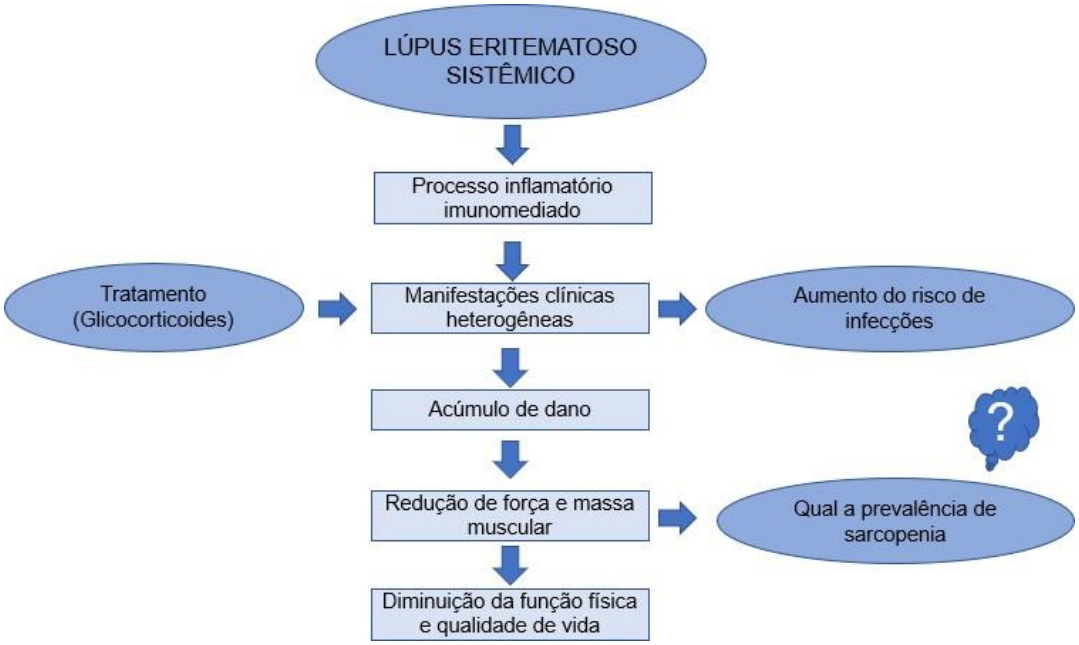
Portanto, apesar de ser um achado clínico que tem um impacto significativo na funcionalidade e qualidade de vida dos pacientes [68], a sarcopenia ainda é um assunto pouco discutido no LES e merece maior atenção.

Justificativa

A sarcopenia é uma doença caracterizada pela baixa força e massa muscular. Além disso, impacta a qualidade de vida dos pacientes e aumenta a incapacidade física, morbidade e mortalidade.

No entanto, a sobreposição da sarcopenia no LES não está bem estabelecida, pois são escassos estudos avaliando este desfecho. Portanto, estudos sobre sarcopenia e desfechos clínicos no LES são necessários a fim de avaliar a prevalência de sarcopenia, bem como suas associações com parâmetros clínicos. Essas associações geram um interesse grande na comunidade cientifica e na prática clínica, a fim de melhorar o manejo da doença e o controle das manifestações clínicas, além da melhora na qualidade de vida e na performance física destes pacientes.

Marco teórico



Objetivos

5.1 Objetivo principal

Avaliar a prevalência de sarcopenia em pacientes com lúpus eritematoso sistêmico.

5.1.2 Objetivos secundários

- Verificar quais critérios de classificação diagnóstica de sarcopenia tem maior sensibilidade e especificidade em pacientes com doença ativa e acúmulo de dano (SLICC/ACR-DI >0).
- Avaliar a associação da sarcopenia com parâmetros clínicos do LES, como: idade, tempo de doença, cronicidade da doença e tratamento farmacológico.

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7. Artigo 1
Systemic Lupus Erythematosus: a systematic review with meta-analysis on muscle strength, muscle mass and physical function.
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Systemic Lupus Erythematosus: a systematic review with meta-analysis on muscle strength, muscle mass, and physical function.

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Abstract

Objective: To perform a systematic review with meta-analysis to verify muscle strength, muscle mass, and physical function of patients with systemic lupus erythematosus (SLE) and compare then with healthy individuals and patients with rheumatoid arthritis (RA).

Methods: A systematic review with meta-analysis of observational studies published in English up to 2022 was performed using MEDLINE (via PubMed) and other relevant sources. Search strategies were based on pre-defined keywords and medical subject headings. The methodological quality of the studies was assessed using the Newcastle-Ottawa Scale. Mean difference (MD) or standardized mean difference (SMD) and 95% confidence intervals (CI) were combined using a random-effects model. Sensitivity analyses were performed when necessary. The significance level was set at $p<0.05$.

Results: The systematic review included 19 studies and the meta-analysis included 11 studies. SLE patients appear to have less muscle strength assessed by handgrip than healthy controls (SLE=21.74kg; healthy controls=29.34kg; $p<0.05$). SLE patients seem

to have greater strength than patients with RA, but this difference was not statistically significant (RA=17.24kg; p=0.210). However, in the sensitivity analysis, SLE group without deforming arthropathy showed higher muscle strength than the RA (p=0.0001). SLE patients with deforming arthropathy have lower muscle strength compared to SLE patients without deforming arthropathy ($p<0.01$). Muscle mass was similar in SLE patients compared to the RA group and healthy controls ($p>0.05$). However, RA patients have a higher BMI than the two groups ($p<0.05$). Patients with SLE have regular physical function.

Conclusion: Muscle strength is affected in SLE patients. SLE patients with deforming arthropathy have less muscle strength than patients without deforming arthropathies.

Keywords: systemic lupus erythematosus, sarcopenia, muscle strength, muscle mass. physical functional performance.

Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease with multisystem involvement [1, 2]. SLE may affect several organs and systems, including the musculoskeletal system [1–3]. Regarding musculoskeletal system, SLE patients have decreased muscle strength when compared to healthy people [4–8]. On the other hand, SLE patients have slightly greater muscle strength when compared to rheumatoid arthritis (RA) patients [5, 8]. However, when SLE patients have deforming arthropathies in the hands, muscle strength is like that of RA patients [5, 9–11].

Some studies describe muscle mass in SLE [6, 12–18]. However, few studies compare muscle mass in SLE patients and healthy controls or SLE patients and AR patients [6, 12–15]. Nevertheless, SLE patients are more likely to have sarcopenia than RA patients [15]. The mechanisms involved in the loss of strength and muscle mass in SLE patients still need to be better elucidated. Changes in muscle strength and muscle mass may lead to sarcopenia. Sarcopenia is a muscle disease (muscle failure) classified into primary sarcopenia and secondary sarcopenia [19, 20]. Primary sarcopenia associates with the aging process [19, 20]. On the other hand, secondary sarcopenia associates with underlying diseases [19, 20]. Therefore, sarcopenia can impair activities of daily living and increase the risk of falls, fractures, hospitalization, and mortality [21–24]. In SLE patients, only one study evaluated sarcopenia [15].

Information on muscle strength, muscle mass, and physical function in SLE patients is scarce. This study aimed to perform a systematic review with meta-analysis to verify the muscle strength, muscle mass (lean mass), and physical function of SLE patients, comparing them with healthy controls and RA patients.

Methods

This systematic review was conducted with meta-analysis in accordance with PRISMA guidelines [25] (supplementary material 1) after registering the protocol in PROSPERO platform (CRDCRD42021242310).

PICO/PECOS format

This systematic review with meta-analysis was based on a focused question described in a PICO/PECOS format [26]. We established Patient/Problem/Population: systemic lupus erythematosus patients; Intervention/Exposure: no interventions; Comparison: healthy individuals or/and patients with other autoimmune diseases; Outcomes: sarcopenia, muscle strength, muscle mass, and physical function; Study: observational and case-control studies.

Data sources

The electronic databases used were: PubMed, Cochrane Library, Cochrane Trials, Cochrane Reviews, Lilacs, and Embase up to April 2022. A comprehensive search strategy tailored to each database was used (supplementary material 2). The authors were contacted, when necessary, for more information on the statistical methodology of the articles chosen as a reference.

Inclusion/exclusion criteria

The Inclusion criteria were: observational (cross-sectional, case-control, and cohort studies); SLE patients; muscle strength, lean mass or physical function data objectively evaluated; and articles written in English language until April 2022. To extract data, only the baseline results from these articles included were collected. A meta-regression comparing the different study designs (cross-sectional, case-control, and cohort studies) was performed. More details are present in the statistical analysis section.

The Exclusion criteria were: studies in experimental models, randomized clinical trials, and reviews; studies on other diseases or data from patients under 18 years old; manuscripts written in a language other than English. There is consensus that Clinical trials are important studies to provide evidence on interventions. However, since we did not aim to evaluate any type of intervention and because the selection process for clinical trials is harder, they were excluded to avoid bias. Therefore, the two clinical trials found were excluded and only observational studies were included in our systematic review and meta-analysis.

Data extraction

Title, abstract, and full text screening was performed in pairs by two independent reviewers (Pena,E and Guaresi,S). The reviewers extracted data from studies independently and disagreements were resolved by discussion. If there was conflict, a third and fourth reviewers (Santo,RCE and dos Santos,LP) provided the final decision. All study data were screened using the bibliographic management program

(Mendeley®, version 1.17.9). The data extracted included author names, publication date, publication journal, number of study participants, population age group, population type, types of muscle strength assessments, muscle mass, physical function, and the results. After agreement between the reviewers and inclusion of the articles in our systematic review with meta-analysis (n=19), data were extracted from each study. When available, data were extracted in the mean form at baseline and standard deviation (SD). When data were not available in the expected format, we contacted the respective authors requesting information about missing data. The, if the authors did not answer or if the data provided by them were unclear, some formulas to standardize the means and SD were used. When data were presented by interquartile range (IQR), they were transformed to standardize the results of all studies in mean change and SD. The equation used to calculate the mean is available below [27].

When data were presented in medians and IQR, we used the following formula [28].

$$xx \approx \frac{qq1 + mm + qq3}{3}$$

Where qq_1 is the first quartile, mm is the median, and qq_3 is the third quartile. Finally, to find the SD presented by IQR, we use the calculation available below [27, 28].

$$\mathcal{SS} \approx \frac{qq_3 - \mathrm{qq}_1}{1.35}$$

A study presented the strength test values in Newtons [7]. To standardize these values with the other articles they were divided by 9.81, converting them to kilograms (kg).Thus, the mean difference (MD) was performed with studies that reported outcomes using the same assessment scale or instrument [29].

Methodological quality assessment

The Newcastle-Ottawa Scale, adapted for cross-sectional studies, was used to assess the methodological quality of the included articles. By using the Newcastle-Ottawa Scale, each study was judged on seven items categorized into three groups: selection of study groups; comparability of groups; and determining the exposure or outcome of interest. The maximum possible score was 10 stars, representing the highest methodological quality [30]. Studies awarded 7 to 10 stars were rated as high quality; 5 to 6 stars as moderate quality; and under 5 stars as low quality [31].

Statistical analysis

For quantitative analysis, the R software version 4.0.5, meta package (version: 5.0-2 command: meta-mean) was used. Meta-analysis was performed to assess the difference on muscle strength and muscle mass of SLE patients, healthy controls, and RA patients. The sensitivity analysis was performed considering patients with or without deforming arthropathy and gender.
Meta-regression analysis was performed to investigate the influence of possible confounding factors, such as disease activity score (SLEDAI), disease duration, age, and gender. A meta-regression comparing the different study designs (cross-sectional, case-control, and cohort studies) was also performed. Moreover, the linear regression test of funnel plot asymmetry was performed to investigate publication bias of studies included.

To all analysis, the summarizing measures (average) and 95% confidence intervals (CI) were estimated by using the random effects model. The heterogeneity of the studies included in the meta-analysis was assessed by the Cochran's Q test and the inconsistency test (I^2). Low, moderate, and high inconsistences were considered the approximated values to 25%, 50%, and 75%, respectively [29–32]. The significance level was set at $p<0.05$.

Results

Search strategy

We identified 538 studies (fig 1). First, we screened the title and abstract of the studies. Then, we included 64 articles for full-text analysis. Lastly, we included 19 studies in the systematic review. We incorporated meta-analysis on 15 studies.

Characteristics of the studies

We included 19 studies published up to April 2022 (table 1). Three of these articles also evaluated patients with rheumatoid arthritis [5, 8, 15]. Two articles evaluated handgrip muscle strength in patients with SLE and deforming arthropathies (Jaccoud arthropathy, mild deforming arthropathy, and erosive arthritis) [9, 10]. Most studies evaluated only women (n=15; 79%) [4–7, 9, 10, 12–15, 17, 18, 33– 35]. On the other hand, four included studies evaluated women and men (n=4; 21%) [8, 16, 36, 37]. The mean age ranged from 29.9 to 47.63 years old. Disease duration ranged from 3 to 17.7 years among patients. According to SLEDAI, SLE had low disease activity.

Systemic lupus activity questionnaire (SLAQ) was assessed in four studies (n=4; 21%) [16, 18, 35, 37]. Three indicated low disease activity [18, 35, 37]. Lastly, one study used the Mix-SLEDAI, one study used the m-SLEDAI, and one study did not report this data (n=3; 15.8%) [5, 10, 33] (table 1). The body mass index (BMI) of the SLE patients was like the healthy controls, with no significant differences ($p>0.05$). The group of patients with RA showed a higher BMI value, which was statistically significant when compared to SLE patients ($p=0.0004$) and healthy controls ($p=0.03$).

Muscle strength

To evaluate muscle strength,11 included studies used the handgrip test: Jamar hydraulic dynamometer, Takei Kiki Kogyo, Grippit instrument, and portable dynamometer. The Jamar manual dynamometer was the most used (n=7; 64%) [7–10, 33, 35, 36], followed by the Takei Kiki Kogyo (n=2; 18%) [6, 34] (Grippit instrument (n=1; 9%) [4], and portable dynamometer (n=1; 9%) [5] (although the equipment is different, all assess the isometric muscle strength of patients' hands).

We performed the meta-analysis with data from all studies included. In the studies of SLE patients, two included patients also with deforming arthropathies [9, 10] and two articles included female and male patients in the same sample [8, 36]. The mean raw (MRAW) of muscle strength among SLE patients was 21.74kg (95%CI, 19.14; 24.34; $I^2=91\%$). In healthy control patients the MRAW was 29.34 kg (95%CI, 26.96; 31.72; $I^2=85\%$), and in RA patients was 17.24 kg (95%CI, 13.13; 21.35; $I^2=78\%$). We found a statistically significant difference between the SLE, RA, and healthy controls ($p<0.05$; fig 2). The control group showed greater muscle strength than both groups. On the other hand, SLE and RA patients had no statistically significant difference in muscle strength ($p=0.210$).

In sensitivity analysis, we excluded studies with patients with SLE and deforming arthropathies (fig 3). The MRAW of muscle strength among SLE patients without deforming arthropathy was 23.52 kg (95%CI, 21.58; 25.46; I^2=85%). SLE patients without deforming arthropathy have lower strength than the control group ($p<0.05$), but greater muscle strength than patients with RA ($p=0.02$).

We also compared SLE groups with deforming arthropathies and SLE without deforming arthropathies in the sensitivity analysis. Muscle strength MRAW among SLE patients without deforming arthropathy was 23.52 kg (95%CI, 21.58; 25.46; I^2=85%). In SLE patients with deforming arthropathy, the MRAW of muscle strength was 15.58 kg (95%CI, 12.33; 18.83; I^2=65%). The groups with and without deforming arthropathies presented a statistically significant difference (supplementary material 3; $p=0.0001$).

Moreover, we performed another sensitivity analysis with studies that included only female patients (with and without deforming arthropathies). The MRAW of muscle strength in SLE women was 20.74 kg (95% CI, 18.21; 23.27; I^2=90%). In the control group (only women), the MRAW was 27.98 kg (95%CI, 26.83; 29.13; I^2=48%). Lastly, the MRAW of muscle strength in the RA women was 15.29 kg (95%CI, 13.02; 17.56; I^2=not applicable). The groups showed a significant difference between the strength values (supplementary material 4; $p<0.01$).

Furthermore, we compared studies in SLE women without arthropathy with healthy control and RA groups. The MRAW of muscle strength of SLE women was 22.71 kg (95%CI, 20.96; 24.46; I^2=81%), lower than the MRAW muscle strength found in the control group (MRAW=27.98 kg; 95%CI, 26.83; 29.13; I^2=48%). On the other hand, the muscle strength in SLE women was greater than muscle strength in RA patients (MRAW=15.29 kg; 95%CI, 13.02; 17.56; I^2=not

applicable). We found a significant difference on the strength values between these groups (fig 4; $p<0.05$).

Lastly, SLEDAI, disease duration, age, gender, and different study designs (cross-sectional, case-control, and cohort) do not influence muscle strength ($p>0.05$) (supplementary material 5 and 6).

Lean mass

To evaluate mass muscle, we used data from five [6, 12–15] studies assessed by lean mass (kg), two by appendicular lean mass divided by height^2 [16, 17], and one by appendicular lean mass divided by fat mass (LMI/FMI) [18]. Three of these studies used dual-energy radiological absorptiometry (DXA) [12–14], one study evaluated muscle mass by bioelectrical impedance (BIA) [15], and one by anthropometric measurements [6]. We did not include three studies in this meta-analysis [16– 18], as they used lean mass adjustments for height or fat mass. In both studies DXA assessed lean mass.

In meta-analysis, the MRAW lean mass in SLE patients was 37.01 kg, (95%CI, 32.05; 41.96; I^2=98%), the MRAW of control group was 38.41 kg (95%CI; 35.32; 41.49; I^2=98%) and the MRAW of patients with RA was 42.60 kg (95%CI; 41.35; 43.85; I^2=not applicable). The RA group may have a greater lean mass when compared to the SLE group, but we found no statistically significant difference between them (fig 5 $p>0.05$).

We did not include three studies in this meta-analysis [16–18] because two assessed muscle mass by appendicular lean mass (LMI) divided by height^2 [16, 17] and one assessed by appendicular lean mass divided by fat mass (LMI/FMI) [18]. The mean of LMI/height^2 in SLE patients were 6.97 kg

[14] and 6.1±1.1 kg [15]. The mean of LMI/FMI in SLE patients was 1.7±0.6 kg.

Physical Function

In this study, we included three studies that objectively measured physical function in patients with SLE [6, 37, 38] and it was impossible to perform the meta-analysis.

Two studies presented physical function data measured by the Short Physical Performance Battery (SPPB). Andrews et al. (2015) showed mean scores of 10.2±1.9 [35] and Plantinga et al. (2018) showed mean scores of 8.8 [37] in patients with SLE. Another study measured physical function by the Timed Up and Go Test (TUG) [6]. The mean of TUG was 5.3±0.4 seconds for SLE patients and 5.0±0.6 seconds for the control group (p=0.049).

Methodological quality of the studies

The supplementary material 7 describes the methodological quality of the included studies. Most studies were classified as high quality.

Publication bias

We found no statistically significant association (p=0.1247), demonstrating no publication bias.

Discussion

This study found that SLE patients showed greater muscle strength than RA patients and lower muscle strength than healthy individuals. However, SLE patients with deforming arthropathy presented similar muscle strength when compared to RA patients. Moreover, patients with SLE and deforming arthropathy in the hands and wrists showed lower muscle strength assessed by handgrip test when compared to patients with SLE without deforming arthropathy. The lean mass was similar between patients with SLE and the control group, but both had lower lean mass compared to RA patients.

Since RA patients present joint deformities, Maria Rydholm et al. (2019) [11] observed that joint manifestations in the wrist and hands such as synovitis, arthritis, joint deformities, pain, and a lower muscle strength in the handgrip test in these patients may be due to mechanical factors. According to the literature, the prevalence of deforming arthropathy in SLE patients varies between 3.47 to 6.2% [39, 40]. Lhakum et al. (2016) found clinical manifestations in the hands and wrists, such as deformities and arthritis in SLE patients [10]. Corroborating with these findings, Lhakum et al. and Loureiro et al. (2020) also detected deformities in the hands and wrists of SLE patients [9]. According to literature, SLE patients may also show joint manifestations. Therefore, we speculate that joint manifestations found in SLE patients by Lhakum et al. (2016) and Loureiro et al. (2020) may influence the muscle strength of these patients.

In our study, we observed that the muscle strength of women with SLE without deforming arthropathy was higher when compared to women with deforming arthropathy. We speculate that deforming arthropathy in SLE may influence the muscle strength measured by the handgrip test in these patients. To evaluate the muscle strength of patients with deforming arthropathies in the hands and wrists would be interesting to use another method of muscle strength assessment. Thus, we could investigate whether the deforming arthropathy

reduces muscle strength or makes it difficult to perform the handgrip test.

Despite the different equipment to assess muscle strength, we methodologically evaluated all tests similarly (isometric strength). The Jamar manual dynamometers are the most cited in the literature and accepted as the gold standard when compared to other dynamometers and equipment [41]. Therefore, the measurements may be considered equivalent [42].

We found one randomized clinical trial in patients with SLE (women>90%), which evaluated muscle strength. We divided the patients into two groups with no clinically significant differences. One group performed a 30-minute daily program of upper limb strengthening and stretching exercises for 12 weeks, and the control group performed four training sessions in alternative methods: daily activities, use of aids, joint protection, and energy conservation. The muscular strength of handgrip at baseline was 22.86±8.77 kg and 21.42±9.75 kg in the respective groups [43]. In our meta-analysis with similar studies (women>90%), the value was 23.52 kg (21.58; 25.46). After the 12-week exercise program, the group that performed upper-extremity strengthening and stretching exercises increased their strength to 26.84±8.92 kg and 29.09±8.52 kg at week six and 12, respectively [43].

A study showed that patients with RA seem to have a higher lean mass value than the other groups. According to the literature, patients with RA also have higher values of body mass index (BMI). The higher the BMI, the greater the musculoskeletal load on the body, requiring a greater demand for systemic muscle strength to perform daily activities, such as locomotion. Moreover, according to Baker et al. (2018) [44], these patients had intramuscular fat, which resulted in low muscle density and, consequently, low muscle strength. The results contributed to our findings that RA patients have lower muscle strength than SLE patients and healthy controls, even though the muscle mass values assessed by DXA seem similar.

Furthermore, Andrews et al. (2015) [18] evaluated SLE patients with a mean age of 46.91±12.7 and did not find associations when comparing body muscle mass and appendicular muscle mass to muscle strength parameters in SLE patients. However, in this study, the lean mass of patients with SLE was like the control group. Thus, we believe that, although SLE is a systemic disease, muscle strength may be affected prior to lean mass. Corroborating this hypothesis, Balsamo et al. (2011) demonstrated that patients with SLE had statistically lower muscle strength and functional performance when compared to healthy individuals [6]. However, lean mass was similar between the SLE group and the healthy group [6].

We also found a clinical trial that evaluated the lean mass of 29 patients with SLE (24 women and five men) that were about to receive high-dose of oral glucocorticoid therapy (prednisolone or equivalent ≥0.5 mg/kg/day for at least six weeks) [45]. The mean age was 39.7±11.5 years old and the mean duration of SLE was 80.1±80 months. By using DXA we assessed lean mass and the baseline value was 35,77±6.47 kg. This lean mass value is like that found in our meta-analysis: 37.01 kg (32.05; 41.96). Lean mass assessed at two and six months after initiation of corticosteroid therapy had a non-significant decrease [45].

The physical function data demonstrated that patients with SLE have regular physical function. However, Andrews et al. (2015) showed that physical function data measured by SPPB in patients with SLE were like those found in healthy patients under 70 years old [46]. Balsamo et al. (2013) [6] found that patients with SLE had worse values of physical performance measured by the TUG test, quality of life, and fatigue assessed by questionnaires reported by SLE patients, when compared to healthy controls. Corroborating this data, Plantinga et al. (2018) found a strong association between lower physical performance measured by the SPPB and worse physical functioning self-reported by SLE patients [37]. The reduction of physical function may harm the patient in their daily

activities, impairing their quality of life. Thus, the physical function is a parameter that needs to be further explored in SLE.

The parameters of muscle strength, muscle mass, and physical function are the current diagnostic criteria for sarcopenia. We found only one study that mentioned sarcopenia in patients with SLE. This study diagnosed, by low muscle mass alone, 10 patients with sarcopenia of 92 patients evaluated [15].

We did not find influence of clinical parameters on muscle strength. We speculate that age did not associate with muscle strength because the patients included in the reviewed studies were mostly young adults (29.9-47.63 years old). Furthermore, SLEDAI did not associate with muscle strength because most patients had low disease activity. Regarding the disease duration, we speculate that it did not influence muscle strength due to the wide variation in the duration of the disease of the included articles. Gender may not have influenced because most articles only included women.

To the best of our knowledge, our study is the first to gather data on muscle strength, muscle mass, and physical function in patients with SLE. We identified the difference in muscle strength between SLE patients with and without deforming arthropathy and we compared these data with RA patients and healthy controls. Furthermore, in SLE patients the muscle mass is like that of healthy controls and lower than in RA patients. This information is important to encourage the practice of physical exercises in patients with SLE.

Limitations

One limitation of our study is heterogeneity. We believe that the high heterogeneity of the samples may be due to different clinical characteristics and countries where the studies were carried out. The comparison of four equipment to measure muscle strength and three methods to measure muscle mass may be a confounding factor and increase the heterogeneity of the groups as well. Another

limitation is that some studies did not mention or separate patients with arthropathy in the hands, which could also be a confounding factor.

Although our systematic review with meta-analysis has limitations, our findings are very important, since SLE is a disease that affects the musculoskeletal system. We found gaps regarding its effects involving muscle strength, muscle mass, and physical function that compose the sarcopenia diagnosis.

Conclusion

In this study, we found that muscle strength is more affected than lean mass in patients with SLE. Moreover, patients with SLE and deforming arthropathy tend to have lower muscle strength than patients without deforming arthropathy. Although encouraging, these data should be evaluated with caution and by prospective studies that assess muscle strength and mass in patients with SLE to better understand the mechanisms involved in these clinical parameters.

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Conflict of interests

The authors declare no conflict of interest.

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Author	Year	Sample	n	Age, years	BMI	Disease duration	Disease activity assessment methods	Disease activity	GCs use (%)	dose of GCs	Antimalarials use (%)	Immunosuppressors use (%)
Andrews et al. [35]	2015	SLE	105	46.4 ± 12.9		14.9 ± 9.2	SLAQ	11.4 ± 7.4	4.8	1-4.5 mg/d		
									21.9	5 - 9.5 mg/d		
									12.4	10 - 14.5 mg/d		
									3.8	15 - 19.5 mg/d		
									1.0	≥ 20 mg/d		
Bağlan Yentür et al. [5]	2018	SLE	46	38.4 ± 10.3		7 ± 4.4						
		Control	46	37.2 ± 8.1								
		RA	51	54.5 ± 12.2		6.6 ± 2.5						
Balsamo et al. [6]	2013	SLE	25	29.9 (6.8)	23.1 ± 2.9	5.3 ± 4.6	SLEDAI	1.5 ± 1.2	84	6.07 ±2.1 mg/d	76	32
		Control	25	29.2 (8.1)	25.5 ± 3.3							
Sola-Rodríguez et al. [34]	2019	SLE	77	43.2 ± 13.8	25.5 ± 4.5	13.9 ± 10.1	SLEDAI	0.68 ± 1.5	100	65 mg/d		
Stockton et al. [7]	2012	SLE	24	39.6 ± 11.4		11 ± 10.4	SLEDAI-2K	4.3 (4.3)	79	6.5 mg/d	67	63
		Control	21	40.9 ± 13.3								
Sumantri et al. [33]	2021	SLE	61	32.66 ± 10.13	23.55 ± 5.4	8 ± 15.5	MIX-SLEDAI	5.08 (3.90)	83.6	5.00 (0.71–46.81) mg/d		
Mahran et al. [8]	2021	SLE	50	39.2 ± 12.5	27.3 ± 6.1	5.3 ± 3.5	SLEDAI					
		Control	50	42.8± 7.09	29.2 ± 4.2							
		RA	50	46.1 ± 12.9	28.3 ± 4.7	9.6 ± 6.9						
Malcus et al. [4]	2008	SLE	71	44.7 ± 14.6		13.9 ± 8.4	SLEDAI					
		Control	71	45.1 ± 14.6								
Keramiotou et al. [36]	2021	SLE	240	47.63 ± 13.01		9.66 ± 8.89	SLEDAI					
		Control	122	47.96 ± 12.67								
Li et al. [12]	2019	SLE	98	46.4 ± 13	22.1 ± 2.6	8 ± 7	SLEDAI-2K	2.5 ± 4.0	71.4	<10 mg/d	78.6	cyclophosphamide: 40.8
		SLE							21.4	10 - 15 mg/d		mycophenolate mofetil: 9.3
		SLE							7.1	>15 mg/d		
		SLE										
		Control	108	47.5 ± 13.2	22.2 ± 2.4							
Liyanage et al. [13]	2013	SLE	27	32.2 ± 8.9	21.2 ± 4.9	3 ± 2.2	SLEDAI	4 (08)		9730 (6160−15,360) mg/d		
		Control	27	33.2 ± 8.2	22.9 ± 4.5							
Seguro et al. [14]	2018	SLE	63	31.14 ± 6.9	25.98 ± 5.0	5.25 ± 3.8	SLEDAI	4.35 ± 5.13		11.60 ± 12.10 mg/d	77.8	82.5

Santos et al. [15]	2011	Control	186	30.68 ± 7.7	24.91 ± 4.9							
		SLE	92	46.8 ± 14.1	27 ± 4.9	9.6 ± 6.9	SLEDAI-2K	2 [4]	56.5	5 (8.8) mg/d	73	33.6
		Control	107	47.5 ± 13.1	26.7 ± 4.7							
		RA	89	49.8 ± 13.8	27.6 ± 5	9.7 ± 7.1			51.7	2.5 (5)		
Loureiro et al. [9]	2020	SLE	22	46.18 ± 12.6		15.41 ± 7.5						
Lhakum et al. [10]	2016	SLE	13	46.7 ± 13.3		6.3 ± 3	mSLEDAI-2K	6.3 (3.0)	100.0	6.4 (3.5) mg/d	30.7	
		SLE	27	43.2 ± 14.1		9.9 ± 8.7	SLEDAI	2.1 (2.0)	88.9	9.2 (5.5) mg/d	22.2	cyclophosphamide: 3.7
		SLE										mycophenolate mofetil: 18.5
Dey et al. [16]	2018	SLE	150	50.1	27.03		SLAQ		88			
Andrews et al. [18]	2015	SLE	102	46.91 ± 12.7		14.6 ± 12.8	SLAQ	11.6 ± 7.5	4.9	1-4.5 mg/d		
									20.6	5 - 9.5 mg/d		
									11.8	10 - 14.5 mg/d		
									3.9	15 - 19.5 mg/d		
									2.0	≥ 20 mg/d		
Plantinga et al. [37]	2018	SLE	60	47.9 ± 12.6		17.7 ± 10.9	SLAQ	16.5 (12.0 – 22.0)				
Elera-Fitzcarrald et al. [17]	2015	SLE	185	34.8 ± 13.8		7.3 ± 6.6	SLEDAI	5.2 (4.3)	83.8	6.2 (4.9) mg/d		

SLE = systemic lupus erythematosus; RA= Rheumatoid arthritis; BMI = Body mass index; SLEDAI =systemic lupus erythematosus disease activity index; SLAQ = systemic lupus activity questionnaire; n = sample size; Values are reported as Mean ± SD unless otherwise stated. Control = health individuals.

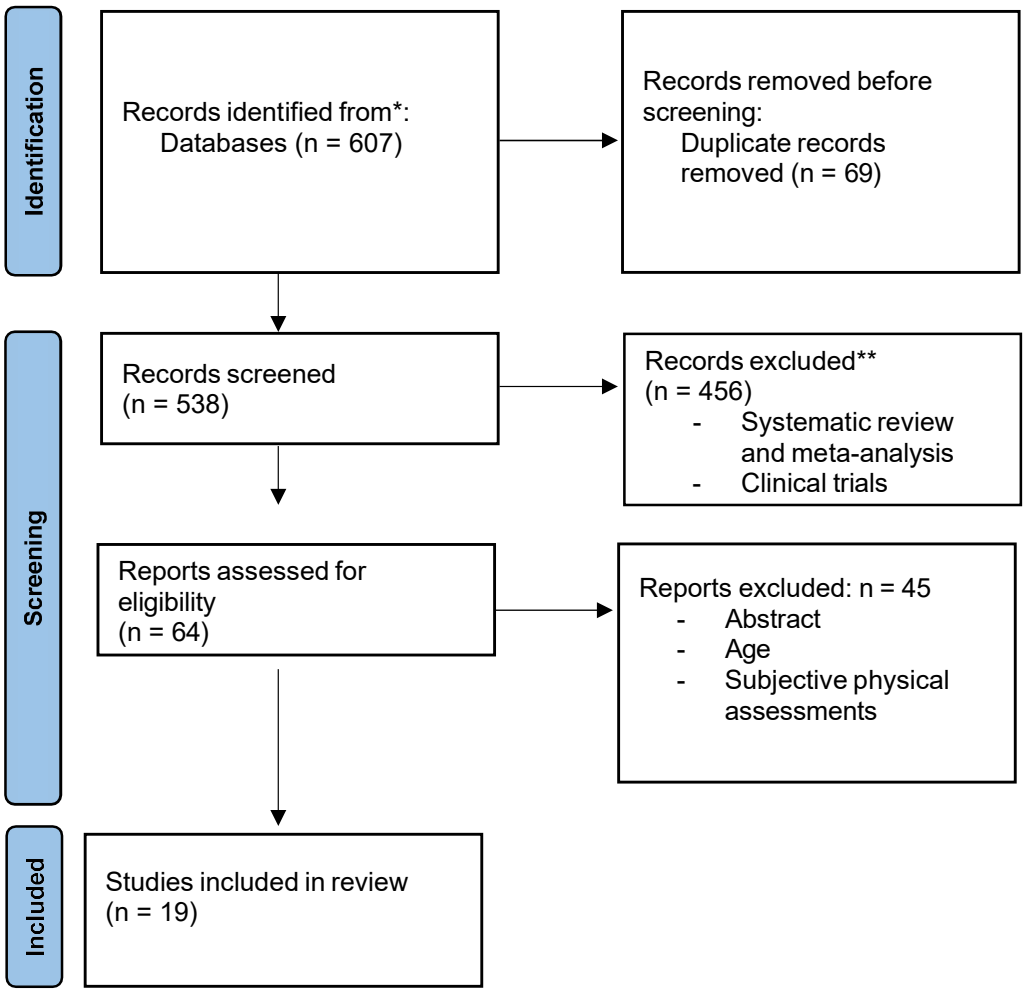


Fig 1 PRISMA. Flow diagram of search results and study selection.

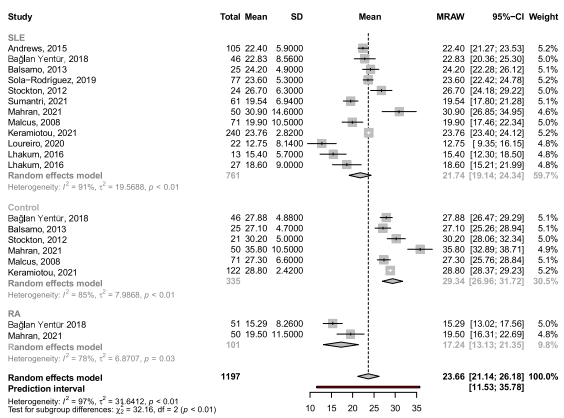


Fig 2 Forest plot of the handgrip strength test including all articles with patients with systemic lupus erythematosus (SLE), control group and the group of patients with rheumatoid arthritis (RA). MRAW, raw mean; ES, estimated; I^2, heterogeneity between studies; CI, Confidence Interval

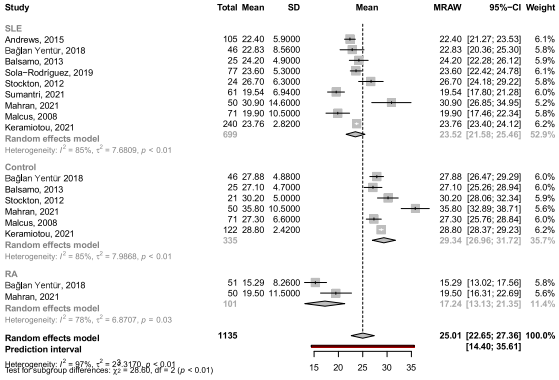


Fig 3 Forest plot of handgrip strength test excluding two studies with patients with systemic lupus erythematosus (SLE) and deforming arthropathies. Including the other studies from the control group and the group of patients with rheumatoid arthritis (RA). MRAW, raw mean; ES, estimated; I^2, heterogeneity between studies; CI, Confidence Interval

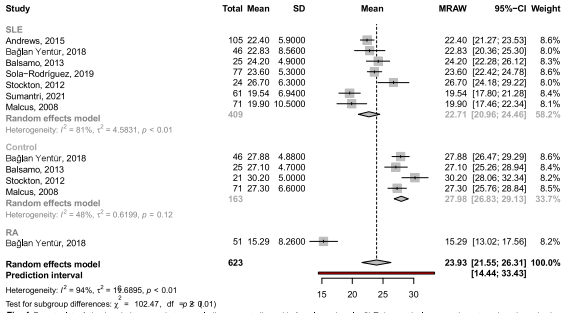


Fig 4 Forest plot of the handgrip strength test excluding two studies with female and male SLE (systemic lupus erythematosus) patients in the same sample and two studies with patients with SLE and deforming arthropathy. Including the other studies from the control group and from the group of patients with rheumatoid arthritis (RA). MRAW, raw mean; ES, estimated; I^2, heterogeneity between studies; CI, Confidence Interval

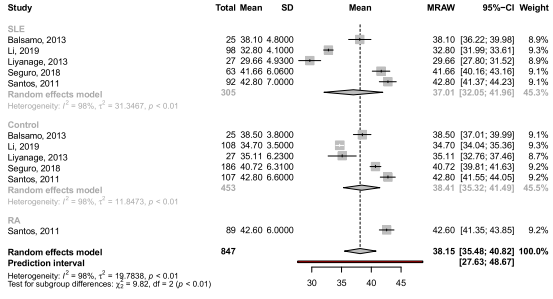


Fig 5 Forest plot of lean mass using body composition (assessed by dual-energy radiological absorptiometry, bioelectrical impedance, or anthropometric measurements) to compare the studies with patients with systemic lupus erythematosus (SLE), control group and the group of patients with rheumatoid arthritis (RA). MRAW, raw mean; ES, estimated; I^2, heterogeneity between studies

PRISMA 2020 Checklist

Supplementary material 1

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4,5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4,5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5,6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify thedate when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each recordand each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6,7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in theprocess.	6,7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in eachstudy were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5,6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	5,6,7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6,7,8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6,7,8
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics andcomparing against the planned groups for each synthesis (item #5)).	5,6,9,10
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or dataconversions.	6,7,8,9
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	6,7,8,9,10
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe themodel(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	6,7,8,9,10
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	8,9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	8,9
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	7,8,9

Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7,8,9

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included inthe review, ideally using a flow diagram.	9
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	6,7,9
Study characteristics	17	Cite each included study and present its characteristics.	9,10
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	6,7,8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision(e.g. confidence/credible interval), ideally using structured tables or plots.	9-14
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	9-14
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	10-14
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	19
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	10-12
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	6-10
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	10-14
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	15-19
	23b	Discuss any limitations of the evidence included in the review.	15-19
	23c	Discuss any limitations of the review processes used.	15-19
	23d	Discuss implications of the results for practice, policy, and future research.	15-19
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	20
Competing interests	26	Declare any competing interests of review authors.	20
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from includedstudies; data used for all analyses; analytic code; any other materials used in the review.	24-36

Supplementary material 2

Search terms Pubmed

("Lupus Erythematosus, Systemic"[mh] OR "Systemic Lupus Erythematosus"[tw] OR "Lupus Erythematosus Disseminatus"[tw] OR "Libman-Sacks Disease"[tw] OR "Libman Sacks Disease"[tw] OR Lupus Nephrit*[tw] OR Lupus Glomerulonephrit*[tw] OR Central Nervous System Lupus[tw] OR Central Nervous System Systemic Lupus[tw] OR Neuropsychiatric Systemic Lupus Erythematosus[tw] OR Lupus Meningoencephalit*[tw])
AND
(sarcopenia[mh] OR sarcopenia*[tw] OR "Physical Functional Performance"[mh] OR Functional Performance*[tw] OR Physical Performance*[tw] OR Muscle function*[tw] OR muscle mass[tw] OR lean mass[tw] OR Physical function*[tw] OR Hand Strength[tw] OR Grip[tw] OR Grips[tw] OR Grasp[tw] OR Grasps[tw] OR Pinch Strength[tw])

Lilacs

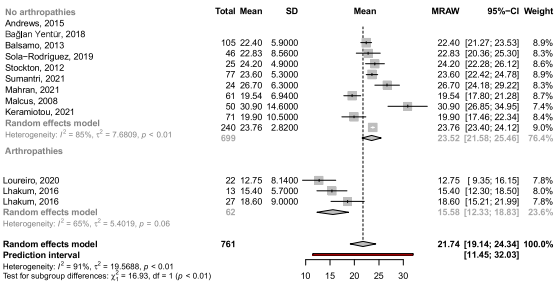
(mh:C20.111.590* OR tw:("Systemic Lupus Erythematosus" OR "Lupus Erythematosus Disseminatus" OR "Lupus Eritematoso Diseminado" OR "Lúpus Eritematoso Disseminado" OR "Libman-Sacks Disease" OR "Libman Sacks Disease" OR "Doença de Libman-Sacks" OR "Enfermedad de Libman-Sacks" OR "Lupus Nephritis" OR "Lupus Nephritides" OR "Lupus Glomerulonephritis" OR "Lupus Glomerulonephritides" OR "Glomerulonefrite Lúpica" OR "Glomerulonefritis Lúpica" OR "Central Nervous System Lupus" OR "Central Nervous System Systemic Lupus" OR "Neuropsychiatric Systemic Lupus Erythematosus" OR "Lúpus Eritematoso Sistêmico Neuropsiquiátrico" OR "Lupus Eritematoso Sistémico Neuropsiquiátrico" OR "Lupus Meningoencephalitis" OR "Lupus Meningoencephalitides"))
AND
(mh:C23.888.592.608.612.500* OR tw:sarcopenia* OR mh:N01.400.545.750* OR tw:("Desempenho Funcional" OR "Desempenho Físico" OR "Desempeño Físico" OR "Desempeño Físico" OR "Rendimiento Funcional" OR "Functional Performance" OR "Physical Performance" OR "Muscle function" OR "muscle mass" OR "lean mass" OR "Physical function" OR "Hand Strength" OR "Aperto de Mão" OR Empunhadura OR Apretón OR Asimiento OR Grip OR Grips OR Grasp OR Grasps OR "Pinch Strength" OR "força de pinça" OR "fuerza de pellizco"))

Embase

('systemic lupus erythematosus'/exp OR 'Systemic Lupus Erythematosus':ti,ab,kw OR 'Lupus Erythematosus Disseminatus':ti,ab,kw OR 'Libman-Sacks Disease':ti,ab,kw OR 'Libman Sacks Disease':ti,ab,kw OR 'Lupus Nephrit*':ti,ab,kw OR 'Lupus Glomerulonephrit*':ti,ab,kw OR 'Central Nervous System Lupus':ti,ab,kw OR 'Central Nervous System Systemic Lupus':ti,ab,kw OR 'Neuropsychiatric Systemic Lupus Erythematosus':ti,ab,kw OR 'Lupus Meningoencephalit*':ti,ab,kw)
AND
(sarcopenia/exp OR sarcopenia*:ti,ab,kw OR 'Physical Performance'/exp OR 'Functional Performance*':ti,ab,kw OR 'Physical Performance*':ti,ab,kw OR 'Muscle function*':ti,ab,kw OR 'muscle mass':ti,ab,kw OR 'lean mass':ti,ab,kw OR 'Physical function*':ti,ab,kw OR 'Hand Strength':ti,ab,kw OR Grip:ti,ab,kw OR Grips:ti,ab,kw OR Grasp:ti,ab,kw OR Grasps:ti,ab,kw OR 'Pinch Strength':ti,ab,kw)

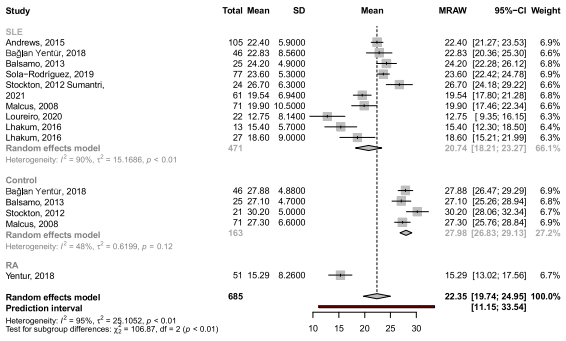
Cochrane's research strategy (trials, protocol and review) are in documents that cannot be converted to PDF.

Supplementary material 3



Forest plot of the handgrip strength test comparing studies with patients with systemic lupus erythematosus (SLE) with or without deforming arthropathies, MRAW, raw mean; ES, estimated; I^2, heterogeneity between studies; CI, Confidence Interval

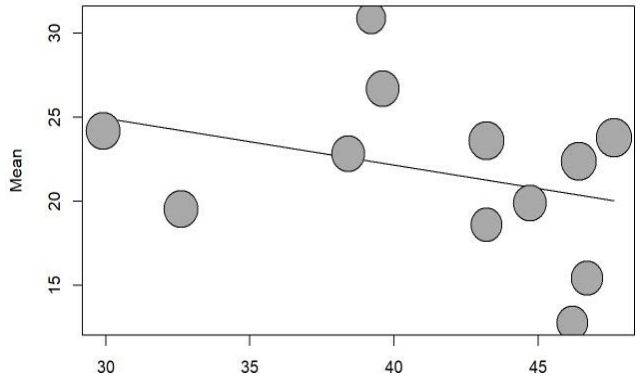
Supplementary material 4



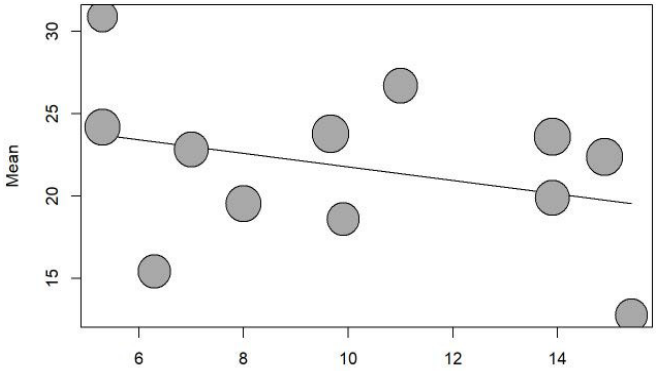
Forest plot of handgrip strength test excluding two studies with female and male SLE (systemic lupus erythematosus) patients in the same sample. Including the other two studies from the control group and from the group of patients with rheumatoid arthritis (RA). MRAW, raw mean; ES, estimated; I^2, heterogeneity between studies; CI, Confidence Interval

Supplementary material 5

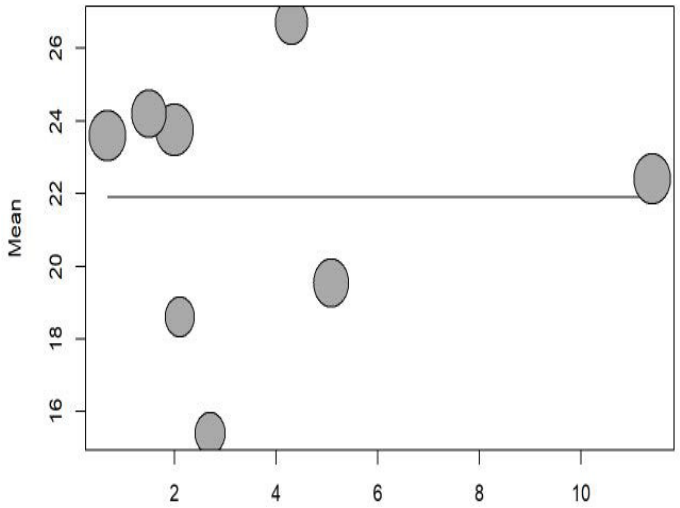
Meta-regression analysis.



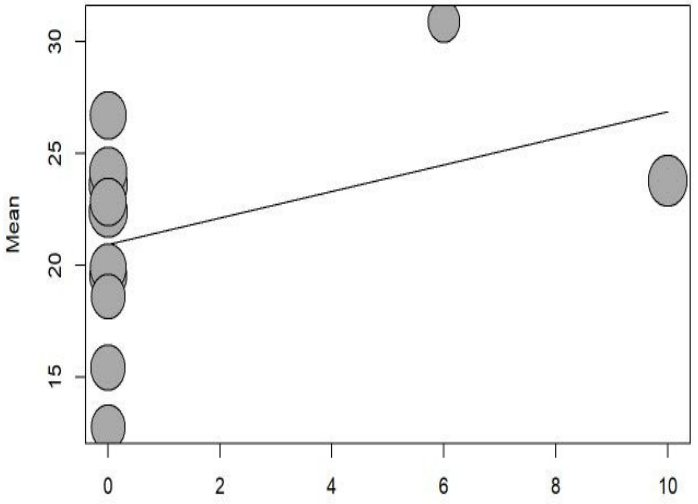
Covariate age (years); p=0.24.



Covariate disease duration; p=0.26.



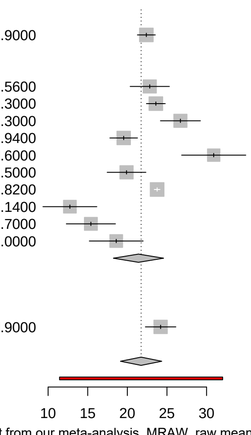
Covariate disease activity score (SLEDAI); p=0.99.



Covariate gender; p=0.14.

Supplementary material 6

Study	Total	Mean	SD	Mean	MRAW	95%−CI	Weight
Cohort							
Andrews, 2015	105	22.40	5.9000		22.40	[21.27; 23.53]	8.9%
Cross−sectional							
Bağlan Yentür, 2018	46	22.83	8.5600		22.83	[20.36; 25.30]	8.3%
Sola−Rodríguez, 2019	77	23.60	5.3000		23.60	[22.42; 24.78]	8.9%
Stockton, 2012	24	26.70	6.3000		26.70	[24.18; 29.22]	8.3%
Sumantri, 2021	61	19.54	6.9400		19.54	[17.80; 21.28]	8.7%
Mahran, 2021	50	30.90	14.6000		30.90	[26.85; 34.95]	7.4%
Malcus, 2008	71	19.90	10.5000		19.90	[17.46; 22.34]	8.4%
Keramiotou, 2021	240	23.76	2.8200		23.76	[23.40; 24.12]	9.0%
Loureiro, 2020	22	12.75	8.1400		12.75	[9.35; 16.15]	7.8%
Lhakum, 2016	13	15.40	5.7000		15.40	[12.30; 18.50]	8.0%
Lhakum, 2016	27	18.60	9.0000		18.60	[15.21; 21.99]	7.8%
Random effects model	**631**				**21.41**	**[18.25; 24.57]**	**82.5%**
Heterogeneity: I^2 = 93%, τ^2 = 24.1366, p < 0.01							
Case−control							
Balsamo, 2013	25	24.20	4.9000		24.20	[22.28; 26.12]	8.6%
Random effects model	**761**				**21.74**	**[19.14; 24.34]**	**100.0%**
Prediction interval						**[11.45; 32.03]**	
Heterogeneity: I^2 = 91%, τ^2 = 19.5688, p < 0.01							
Test for subgroup differences: χ^2_2 = 3.25, df = 2 (p = 0.20)							



Forest plot comparing different study designs that include the handgrip test from our meta-analysis. MRAW, raw mean; ES,estimated; I²,helerogeneity between studies;CI,Confidence Inlerval.

Supplementary material 7.

Table 2. Description of quality assessment using the Newcastle-Ottawa Scale.

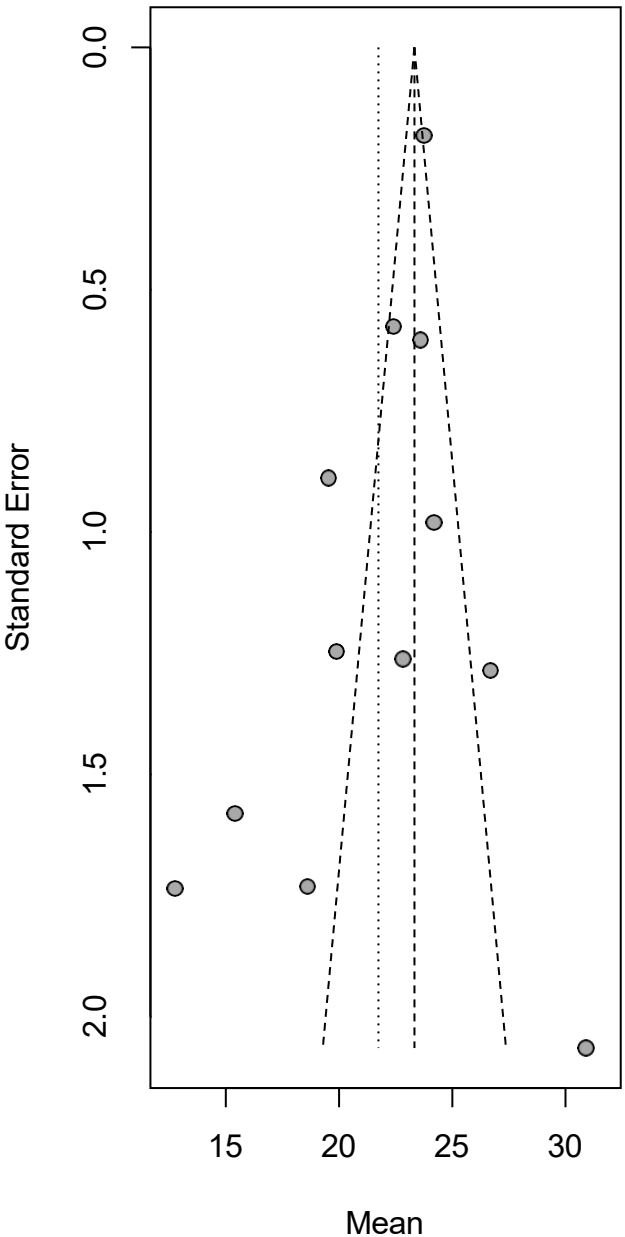
First author name	Year	Selection (1-5 stars)	Comparability (1-2 stars)	Outcome (0-3 stars)	Overall NOS (1–10 stars)
Andrews et al. (35)	2015	***		**	5
Bağlan Yentür et al. (5)	2018	****		***	7
Balsamo et al. (6)	2013	*****	**	**	9
Sola-Rodríguez et al. (34)	2019	****		***	7
Stockton et al.(7)	2012	*****		***	8
Sumantri et al. (33)	2021	****	**	***	9
Mahran et al. (8)	2021	*****	*	***	9
Malcus et al. (4)	2008	*****		**	7
Keramiotou et al. (36)	2021	*****		***	8
Li et al. (12)	2019	*****	**	***	10

Liyanage et al. (13)	2013	*****		***	8
Seguro et al. (14)	201	****	*	***	8
Santos et al. (15)	2011	****	**	***	9
Loureiro et al. (9)	2020	****		***	7
Lhakum et al. (10)	2016	***		***	6
Dey et al. (16)	2018	***		**	5
Andrews et al. (18)	2015	****		**	6
Plantinga et al. (37)	2018	***		*	4
Elera-Fitzcarrald et al. (17)	2017	****		**	6

Asterisks (*) Represents the number of "stars" of quality Newcastle-Ottawa Scale (NOS).

Supplementary material 8

Linear regression test of funnel plot asymmetry.



p=0.12.

Artigo 2

Prevalence of sarcopenia in women with systemic lupus erythematosus

Periódico: Lupus Science e medicine

Status: Submission

Prevalence of sarcopenia in women with systemic lupus erythematosus.

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Abstract

Objective: To assess the prevalence of sarcopenia in SLE patients and its associations with clinical parameters.

Methods: In this cross-sectional study, women with SLE (18 to 50 years old) were included. The following data were collected: disease duration, disease chronicity (SLICC/ACR-DI), disease activity (SLEDAI-2k), treatment regimen, quality of life (SLEQoL), physical activity level (IPAQ), muscle strength by handgrip and chair stand tests, muscle mass by dual-energy radiological absorptiometry (DXA). Muscle mass was evaluated by 3 different parameters [appendicular skeletal muscle mass (ASM), ASM/height² and ASM/BMI]. Physical performance was evaluated by the Timed-up-and-go (TUG) and Short Physical Performance Battery (SPPB) test. The descriptive analysis, Pearson's or Spearman's correlation coefficients, Sensitivity analysis and Chi- squared test were performed. The significance was considered $p<0.05$.

Results: Forty-nine patients were included [median age: 35.0 (28.0–43.5) years; median disease duration: 8.0 (4.0–14.5)] years. Chronicity and disease activity were low. The patients presented muscle strength by the handgrip test of 24.71±9.01 kg and 14.32±3.68 seconds using the chair stand test. The patients had muscle mass assessed by the ASM of 17.03±2.32 kg, ASMI 6.70±0.88 kg and ASM/BMI 0.63±0.11 kg. Physical performance was preserved in these patients. The prevalence of sarcopenia was 16.3% following the European Working Group on Sarcopenia in Older People-2 (EWGSOP2) criteria (chair stand test and ASM). There was no association between sarcopenia and age, disease duration, disease chronicity, disease activity, cumulative corticosteroid dose, quality of life, and physical activity level ($p>0.05$).

Conclusion: The prevalence of sarcopenia was 16.3% in SLE patients. However, sarcopenia is not associated with clinical parameters. Therefore, more studies should be developed to evaluate risk factors of sarcopenia in SLE patients.

Keywords: Systemic lupus erythematosus, sarcopenia, muscle strength, muscle mass, physical performance.

Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease with multisystem involvement [1,2]. The SLE may affect several organs and systems, including the musculoskeletal system [1–3]. Studies show that patients with SLE have decreased muscle strength compared to healthy people [unpublished data]. In regarding to skeletal muscle mass, there are few studies that describe this outcome in SLE compared to healthy controls. However, the data are controversial and different methods were used to assess muscle mass [unpublished data]. Physical performance has been objectively evaluated in previous studies and their results suggest a regular course.

Changes in muscle strength and muscle mass may lead to sarcopenia [4]. Sarcopenia is considered a muscle disease (muscle failure), characterized by decreased muscle strength and muscle mass. Its severity is perceived through objective physical performance tests. Sarcopenia usually develops as a consequence of age-related decline. Such a condition is termed as primary sarcopenia. On the other hand, if the cause of the condition is another disease, it is termed secondary sarcopenia [4].

Only one study assessed sarcopenia in LES, where only body composition was measured. The cutoff to define sarcopenia was a fat free mass index ≤2 standard deviations (SD) below the mean of a reference Caucasian population. Santos et al (2011) assessed 92 women with SLE, 89 with rheumatoid arthritis (RA) and 107 controls, and demonstrated that sarcopenia prevalence was found in 10.9%, 4.5% and 6.5%, respectively [5]. Due to the lack of research about sarcopenia in LES, our objectives were: (1) to assess the prevalence of sarcopenia according to different diagnostic classification criteria (EWGSOP2), (2) to verify which of these diagnostic classification criteria is more sensitive and specific for patients with cumulative damage from SLE, and (3) to assess the relationship between the prevalence of sarcopenia and clinical parameters.

Methods

Study design

This is an observational, exploratory and cross-sectional study evaluating changes in muscle strength, muscle mass and physical performance in women with SLE. We reported this study according to STROBE checklist for cross-sectional study [6].

Settings

Patients were recruited through the rheumatology service at a public hospital in Rio Grande do Sul, Brazil (Hospital de Clínicas de Porto Alegre, HCPA) between April 2021 and August 2022. The institutional review board of the Universidade Federal do Rio Grande do Sul, Hospital de Clínicas de Porto Alegre, Brazil (registered under number 20-0576) approved this study, and the declaration of Helsinki principles were followed. Data collection was composed by clinical features, assessment of muscle strength, muscle mass and physical performance

Participants

Forty-nine patients diagnosed with systemic lupus erythematosus according to the Systemic Lupus International Collaborating Clinics (SLICC-2012) and aged between 18 and 50 years old were included. We excluded patients with dysphagia; illicit drug use or alcohol abuse (self-reported by patient, characterized by the ingestion of three or more drinks a day or seven or more drinks a week, each serving being equivalent to 330 ml of beer or 150 ml of wine or 45 ml of distillate); severe chronic heart failure defined as New York Heart Association [(NYHA) class 3 or 4]; severe chronic obstructive pulmonary disease [mMRC ≥ 2 (modified medical research council)]; chronic kidney disease [with mean CKD-EPI creatinine clearance < 30ml/min/1.7² (*Chronic Kidney Disease Epidemiology Collaboration)];* diabetics; uncompensated thyroid; history of cancer in the last five years (except non-melanoma skin cancer); other rheumatic disease; myositis; chronic viral, bacterial and fungal infections; history of locomotor system surgery in the last year; clinical or surgical complications with need hospitalization for more than seven days in the last 6 months; pregnant and lactating women; patients with deformities in the lower and upper limbs (bone erosions that make it impossible to carry out the data collection protocol);

osteonecrosis of any site; patients with a history of resistance exercise, supervised or not by physicians or physical therapists, for a period of 12 or more weeks of training, in the last 6 months.

Data collection

We collected data such as: clinical features (age, diagnosis, disease duration, disease activity, cumulative disease damage, pharmacological treatment), tobacco use, physical activity level, quality of life, muscle strength, body composition and physical performance.

Clinical features

Clinical data were collected through the electronic medical record, such as: age (years old), disease duration (years), presence of current smoking, and pharmacological treatment (corticosteroid therapy). Disease activity was assessed by “The Systemic Lupus Erythematosus Disease Activity Index 2000” (SLEDAI-2k). The SLEDAI-2K is classified as follows: LES inactive: 0; mild activity: 1-5; moderate activity: 6-10; high activity: 11-19; and very high activity: 20 or more [7]. Cumulative disease damage was assessed using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR-DI) questionnaire [8]. Physical activity was measured using the International physical activity questionnaire (IPAQ) and quality of life was assessed using the Systemic Lupus Erythematosus Quality of Life Questionnaire (SLEQoL) [9,10].

Muscle strength

Muscle strength of the upper limb was assessed by the handgrip test (Jamar® dynamometer). The maximum strength reached by the subjects during the three attempts of maximum isometric contraction was used as a reference for the analysis of the maximum isometric strength [11,12]. This method has its reliability tested inter and intra evaluators [12]. Handgrip strength values <16 kg for women was considered indicative of low muscle strength [4]. The strength of the lower limb was evaluated by the chair test. This test consists of the patient performing 5 movements of sitting and standing in a chair. Low muscle strength was >15 seconds considered [4].

Muscle mass

To assess muscle mass, a dual X-ray absorptiometry examination (DXA; HOLOGIC, fambeam 4500A) was performed [13–15] . The appendicular skeletal muscle mass (ASM) was obtained from the sum of arms and legs muscle mass. The appendicular skeletal muscle mass index (ASMI) was obtained from ASM height squared (ASM/height^2). The cut-off point considered for low muscle mass was <15 kg (ASM) and <5.5 kg/m² (ASMI) [4]. In addition, body mass index (BMI) was calculated by total body weight (kg) divided by squared height². We also adjusted the ASM by the patients' BMI [16,17].

Physical performance

The physical performance was assessed by short physical performance battery (SPPB) and timed up and go (TUG) test. SPPB consists of performing balance activities, sitting and standing up from a chair and walking 3 meters. Each test is counted through a score and the higher this value, the better the result. The rating can range from 0 to 12 points [18]. The TUG consists of the patient getting up from a chair, walking to a reference point, positioned 3 meters away, turning around, returning and sitting down in the chair again [19]. The time the patient takes to complete these routes is checked. The cutoff points considered for low physical performance by SPPB and TUG are: ≤8 point score and ≥20 seconds, respectively [4].

Diagnosis of sarcopenia

Sarcopenia was diagnosed by the European Working Group on Sarcopenia in Older People (EWGSOP2) criteria for women [4]. The diagnosis of sarcopenia was made based on the assessment of muscle strength and muscle mass. To assess the severity of sarcopenia, the physical performance of patients was evaluated. The cut-off point for low muscle strength assessed by the handgrip test was <16 kg and for the chair stand test it was >15 seconds for 5 repetitions (criteria 1). For low muscle mass, the cutoff point was considered <15 kg for ASM and <5.5 kg for ASMI (criteria 2). In addition, we also used the ASM/BMI correction, where the cut-off point is <0.512 for women (criteria 2). To classify the severity of sarcopenia, the cutoff point was TUG>20 seconds and SPPB ≤8 points (criteria 3). Therefore, Probable Sarcopenia is identified by

criterion 1. The diagnosis is confirmed by additional criterion 2 documentation. If Criteria 1, 2, and 3 are met, the sarcopenia is considered severe.

Statistical analysis

The sample size calculation was based on a study that showed a 35% prevalence of sarcopenia in patients with RA [20]. There is a study that evaluated the prevalence of sarcopenia in patients with SLE. However, the diagnosis of sarcopenia was based on a criterion not currently used. Nevertheless, we chose to use this meta-analysis with patients with RA.

Assuming a population of 80 patients being followed up at the Systemic Lupus Erythematosus outpatient clinic of the Hospital de Clínicas de Porto Alegre (HCPA), with a prevalence of sarcopenia at 35% in RA patients, 5% confidence interval and effect of design 1.0, the sample size calculation of 66 patients will be sufficient for the present study. The sample size calculation was performed using the OpenEpi software (version 3). The Shapiro–Wilk method was used to test for normality. Results are expressed as mean ± standard deviation (SD), median (interquartile range), and number (%), as appropriate. Pearson's or Spearman's correlation coefficients were explored to assess the associations between the prevalence of clinical parameters and muscle mass (ASM, ASMI and ASM/BMI) with muscle strength and physical function.

Lastly, we performed sensitivity and specificity analysis between diagnostic classification criteria for sarcopenia and patients with disease damage and the chi-square test for association between sarcopenia criteria and clinical parameters. The significance was considered $p<0.05$.

Results

Clinical features

Sixty patients were recruited. However, 5 patients with overlapping systemic sclerosis, 4 patients had overlapping fibromyalgia, and 2 patients had hip osteonecrosis were excluded. Thus, our sample consisted of 49 patients included. The median (IQR) age was 35.0 (28.0–43.5) years old and the median disease duration was 8.0 (4.0–14.5) years. The disease activity measured by SLEDAI-2k was considered low, with a median of 2.0 (0.0–4.0). The chronicity index of the disease measured by the SLICC/ACR was median 0.0 (0.0 –1.0). Eighteen patients (36.73%) had SLICC>0. Among these 18 patients, 1 patient

(2.04%) had musculoskeletal damage. The cumulative corticosteroid dose was calculated from the last 12 months. Twelve patients were on glucocorticoid treatment in the last 12 months, with a median cumulative dose of 2.73 (1.18–6.63) grams. The median BMI was 25.44 (23.14–29.88). In regard to physical activity level, 83.7% of patients had low physical activity, 12.2% moderate and 4.1% a high. These data, as well as other clinical data, are described in Table 1.

Table 1. Descriptive data of clinical characteristics in SLE patients.

	n	SLE patients
Age (Year), median (IQR)	49	35.0 (28.0–43.5)
Ethnicity, n (%)		
Caucasian	27	55.1 %
Black	7	14.3 %
Brown	15	30.6 %
Disease duration(years), median (IQR)	49	8 (4.0–14.5)
SLEDAI-2k, median (IQR)	49	2 (0.0–4.0)
SLICC/ACR-DI, median (IQR)	49	0 (0.0–1.0)
Corticosteroid		
12 months (grams), median (IQR)	12	2.73 (1.18–6.63)
6 months (grams), median (IQR)	12	1.35 (0.54–3.12)
BMI, median (IQR)	49	25.44 (23.14–29.88).
SLEQoL, mean ± SD	49	131.41±45.43
IPAQ (min/week), median (IQR)	49	583.60 (0.00–409.50)
Low level of physical activity	41	83.7%
Moderate level of physical activity	6	12.2%
High level of physical activity	2	4.1%

SLEDAI-2k= *The Systemic Lupus Erythematosus Disease Activity Index 2000;* SLICC/ACR= Lupus International Collaborating Clinics/American college of rheumatology damage index; BMI = body mass index/height²; g= grams; SLEQoL= systemic lupus erythematosus quality of life questionnaire; IPAQ= International physical activity questionnaire; METs= Metabolic equivalent of task. Results are expressed as mean ± standard deviation (SD) or median (interquartile 25%-75%).

Strength, muscle mass and physical performance

The mean of muscle strength evaluated by the handgrip test was 24.71±9.01 kg and the muscle strength by the chair stand test was 14.32±3.68 seconds. Eight patients (16.3%) showed low muscle strength by the handgrip test and twenty-four patients (49%) showed low muscle strength by the chair stand test.

The mean of muscle mass evaluated by ASM was 17.03±2.32 kg. When adjusted for height² (ASMI), the mean was 6.70±0.88 kg and when adjusted for BMI (ASM/BMI) the mean was 0.63±0.11. The low muscle mass assessed by ASM, ASMI and ASM/BMI were found in 10 patients (20.4%), 3 patients (6.1%) and 8 patients (16.3%), respectively.

The median of physical function evaluated by the SPPB was 10.0 (10.0-11.0) points and the TUG test was 7.43 (6.78-8.64) seconds. All patients demonstrated good physical performance by SPPB score (>8 points) and by TUG (time <20 seconds).

Table 2. Descriptive data on muscle strength, muscle mass and physical performance.

Outcomes	N	
Strength Muscle		
Handgrip test, mean ±SD, Kg	49	24.71±9.01
>16 kg	41	83.7%
<16 kg	8	16.3%
Chair stand, median (IQR), sec	49	17.03±2.32
>15 sec	24	49 %
<15 sec	25	51 %
Muscle Mass		
ASM, mean ±SD, Kg	49	17.03±2.32
> 15 kg	39	79.6 %
< 15 kg	10	20.4%
ASMI, mean ±SD, Kg	49	6.70±0.88
> 5.5 kg	46	93.9%
< 5.5 kg	3	6.1%
ASM/IMC, mean ±SD	49	0.63±0.11
> 0.512	41	83.7%
< 0.512	8	16.3%
Physical performance		
SPBB, median (IQR)), point >8	49	10.0 (10.0–11.0)
	49	100 %
TUG, median (IQR), sec < 20 sec	49	7.43 (6.78–8.64)

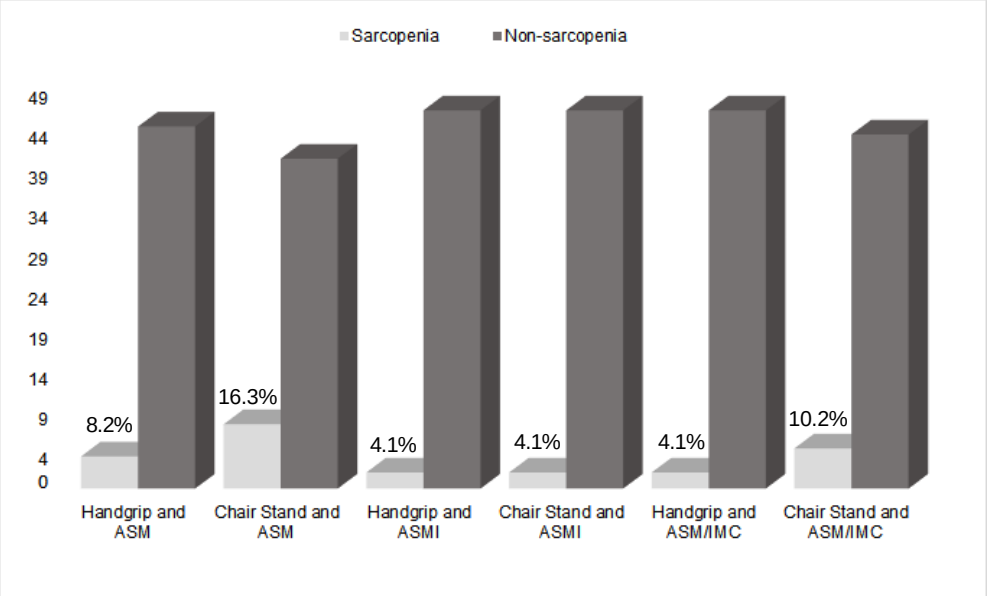
49 100%

ASM= Appendicular skeletal muscle mass; ASMI= Appendicular skeletal muscle mass index; ASM/BMI= Appendicular skeletal muscle mass adjusted by body mass index. Results are expressed as mean ± standard deviation (SD) or median (interquartile 25%–75%).

Prevalence of sarcopenia

Sarcopenia ranged from 4.1% to 16.3% according to the diagnostic criteria used. The highest prevalence found was 16.3%, when diagnosed by the chair stand test and the appendicular skeletal muscle mass (ASM), with the cutoff points recommended by the EWGSOP2.

Figure 1. Prevalence of sarcopenia in SLE patients according to different criteria



ASM = appendicular skeletal muscle mass; ASMI= appendicular skeletal muscle mass adjusted for height²; ASM/BMI = appendicular skeletal muscle mass adjusted for BMI.

In the sensitivity and specificity analysis of diagnostic criteria for sarcopenia in patients with cumulative SLE damage assessed by SLICC/ACR-DI, our results show that the diagnosis of sarcopenia evaluated by chair stand test and ASM showed more sensitivity (28%) for patients with SLICC/ACR-DI >0. More details are described in table 3.

Table 3. Sensitivity and specificity of sarcopenia criteria for patients with SLICC>0.

Diagnostic Sarcopenia	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Handgrip and ASM	17% (4–42)	97% (81–99)	75% (22–97)	66% (51–80)
Chair stand and ASM	28% (11–54)	90% (74–97)	62% (26–90)	70% (52–81)
Handgrip and ASMI	5% (0.3–24)	96% (81–99)	50% (26–97)	64% (50–77)
Chair stand and ASMI	11% (1–36)	100% (86–100)	100% (18–100)	66% (58–79)
Handgrip and ASM/BMI	0% (0–22)	93% (77–99)	0% (0–80)	62% (46–75)
Chair stand and ASMI/BMI	5% (3–29)	87% (70–96)	20% (1–70)	61% (45–75)

Results are expressed as percentage (%) and interquartile 25%–75%.

Lastly, we performed the chi-square test to associate the diagnosis of sarcopenia (chair stand and ASM) with age, disease duration, SLICC/ACR-DI, sledai-2k, SLEQoL, IPAQ, and corticosteroid therapy. None of these clinical variables showed a statistically significant difference ($p>0.05$).

Discussion

To the best of our knowledge, our study is the first to assess the prevalence of sarcopenia in patients with SLE following current diagnostic criteria (EWGSOP2). In our study, we found the prevalence of 16.3% of sarcopenia in patients with SLE (chair stand test and ASM). Most patients have muscle strength and muscle mass above the sarcopenia cutoff. As for muscle mass, patients have less muscle mass by ASM than by ASMI or ASM/BMI.

In our study, patients demonstrated muscle strength by handgrip test similar to that found in our systematic review article with meta-analysis 24.71±9.01 kg and 22.71 kg (20.96–24.46), respectively [unpublished data]. In addition, 16.3% of the patients showed low muscle strength by the handgrip test (<16 Kg; EWGSOP2). However, when muscle strength was assessed by chair stand test, 49% of patients demonstrated low muscle strength (>15 sec; EWGSOP2). Although the patients were young adults with low disease duration, disease chronicity and disease activity, we believe it is important to assess and monitor the muscle strength of SLE patients in clinical practice.

As for the different ways of assessing muscle mass, the EWGSOP2 recommends the assessment of muscle mass through skeletal muscle mass (ASM) and with height² adjustment (ASMI). In addition, other indices are common in the literature, such as the ASM adjusted by the body mass index (BMI). In our

findings, patients had showed lower total appendicular skeletal muscle mass (20.4%) than when adjusted for height² (6.1%) or BMI (16.3%). Kim et al., (2016) evaluated women over 65 years of age and compared the diagnosis of sarcopenia with 3 ASM adjustments (ASMI, ASM/BMI, and ASM/weight) [16]. The authors mention that adjustments for muscle mass may influence the prevalence of sarcopenia, as well as aging. In addition, the ASM/BMI adjustment presents a prevalence of sarcopenia greater than twice when compared to the prevalence by ASMI [16]. This result corroborates our findings, where the prevalence of sarcopenia assessed by chair stand test and ASM/BMI was 10.2% and ASM/height² was 4.1%. Furthermore, the adjustment ASM/BMI versus ASMI showed low muscle mass in 16.3% and 6.1% of patients, respectively.

In addition, our patients had good physical function assessed by SPPB and TUG. These data corroborate the data from previous studies published by Andrews et al., (2015) and Balsamo et al., (2013) [21,22]. Plantinga et al. (2018) found a SPPB value of 8.8 points, but the evaluated patients had a mean age (47.9±12.6) and disease duration (17.7±10.9), these are values higher than what we found [23].

In our study, we found the prevalence of 16.3% of sarcopenia in patients with SLE (chair stand test and ASM). There is only one study that assessed the prevalence of sarcopenia in SLE patients [5]. Santos et al. (2011), estimated the prevalence of sarcopenia through the electrical bioimpedance exam and used only the low lean mass index divided by height² as diagnostic criteria. Women with values ≤13.4 kg were considered sarcopenic [4]. The prevalence of sarcopenia in SLE patients found in accordance with Santos et al., (2011) was 10.9% [5]. In a review, Santo et al., (2022) summarized the evidence on sarcopenia in patients with rheumatic diseases [24]. In patients with RA, the prevalence of sarcopenia ranges from 4.6% to 37.1%. In patients with systemic sclerosis, the prevalence of sarcopenia ranges from 15.9% to 42% and in patients with spondyloarthritis the prevalence ranged from 0% to 62% [24]. The higher variation between prevalence of sarcopenia may be explained due to the diagnostic classification criteria used, methods of assessment, as well as the characterization of population.

According to the Pinto et al., (2017) patients with SLE have more sedentary time and are more inactive than the general population [25]. Corroborating with the literature, most of our patients had a low level of physical activity (83.7%). It is know that, higher levels of physical activity were associated with better physical function and less fatigue and pain in SLE patients [26]. Physical inactivity is related to increased proinflammatory cytokines, decreased energy expenditure, production of rapid skeletal muscle insulin insensitivity, reduction of protein synthesis and selective loss of thin (actin) over thick (myosin) filaments, as well as other changes. Furthermore, it is known that low levels of physical activity and physical exercise, may to impact the onset and worsening of sarcopenia [24,27,28].

There are no longitudinal studies evaluating the impact of sarcopenia on the clinical parameters of patients with SLE. In our cross-sectional study, we did not find associations between the diagnosis of sarcopenia and clinical parameters, because of our low number of patients included, being young adults, having short disease duration and low disease chronicity and activity. However, we speculate that, as observed in other rheumatic diseases, sarcopenia may influence the worsening of the activity and chronicity of the disease, worsening quality of life and increasing morbimortality [24].

Limitations

Our study has some limitations. One limitation is that we do not have a group of healthy women to compare the data collected. In addition, our exclusion criteria led to inclusion of patients with less aggressive disease. It is known that the cumulative damage of the SLE usually reflects in damage to the musculoskeletal system [29]. Therefore, we believe it is necessary to evaluate the prevalence of sarcopenia in SLE patients with greater disease activity and chronicity. In addition, not reaching the proposed sample size can be another limitation. However, our findings are important for clinical practice in order to provide data on SLE patients that are scarce in the literature.

Conclusion

The prevalence of sarcopenia was 16.3% in patients with SLE. The diagnosis of sarcopenia assessed by the chair stand test and ASM demonstrated to be more sensitive (28%) for patients with cumulative disease damage. In contrast, no association of clinical parameters with sarcopenia was found. Therefore, longitudinal studies should be developed to assess risk factors for sarcopenia in patients with SLE.

Acknowledgments

We wish to thank the Fundo de Incentivo à Pesquisa e Eventos (FIPE) of the Hospital de Clínicas de Porto Alegre and the research support fund of the Sociedade de Reumatologia do Rio Grande do Sul for the financial support.

Conflict of interests

None conflict of interest.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2,3
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
Methods			
Study design	4	Present key elements of study design early in the paper	1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3,4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3,4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4,5,6*
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	6,7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6,7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6,7
		(*b*) Describe any methods used to examine subgroups and interactions	6,7
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7,8
		(b) Give reasons for non-participation at each stage	3,4,,7, 8
		(c) Consider use of a flow diagram	3
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each	7,8

		variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	7-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5,6,10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Considerações finais

Com base nos achados da nossa revisão sistemática com meta-análise, os pacientes com LES parecem ter menos força muscular do que controles saudáveis e maior força muscular, mesmo que não estatisticamente significativo, que pacientes com AR. Pacientes com LES com artropatia deformante apresentam menor força muscular do que pacientes com LES sem artropatia deformante. A massa muscular não demonstrou diferença estatisticamente significativa entre os grupos LES, controle e AR e a performance física parece estar regular em pacientes com LES.

No estudo transversal, a prevalência de sarcopenia em pacientes com LES foi de 16,3%; O critério de classificação diagnóstica de sarcopenia avaliado pelo teste de sentar-se e levantar-se da cadeira e da massa muscular apendicular esquelética, apresentou maior sensibilidade para encontrar pacientes sarcopênicos com dano cumulativo do LES; não foi encontrado associação da sarcopenia com idade, tempo de doença, atividade e cronicidade da doença, SLEQoL, IPAQ e tratamento farmacológico.

Perspectivas futuras

As perspectivas futuras deste estudo são:

- Acompanhar esses pacientes de forma longitudinal, a fim de avaliar a incidência de sarcopenia e verificar fatores de risco para sarcopenia.
- Incluir mais pacientes para atingir nosso tamanho de amostra estimado (66 pacientes).
- Realizar as análises de marcadores de perda de massa muscular nas amostras de sangue e urina armazenadas.

Além disso, no período de delineamento do presente estudo, estabelecemos uma parceria com um grupo de pesquisa do Hospital das Clínicas da Universidade Federal de Minas Gerais. Nosso objetivo é ampliar este projeto em outros centros de pesquisa.

ANEXOS

ANEXO I

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

GPPG ou CAAE: 40406920.6.0000.5327

Título do Projeto: Sarcopenia em pacientes com Lúpus Eritematoso Sistêmico - Um estudo transversal.

Você está sendo convidado(a) a participar de uma pesquisa cujo objetivo é avaliar componentes como ossos, musculatura e gordura corporal, além de capacidade física, força muscular, cansaço durante o exercício, substâncias no sangue e na urina que mostram como o lúpus eritematoso sistêmico influência na função física a longo prazo. Esta pesquisa está sendo realizada pelo Serviço de Reumatologia do Hospital de Clínicas de Porto Alegre (HCPA).

Se você aceitar o convite, serão realizadas coletas de dados clínicos do seu prontuário eletrônico como: idade, duração da doença (anos), presença de tabagismo atual, fator reumatóide, anticorpos anti-citrulinados de proteínas, erosões ao RX simples e tratamento farmacológico. Além disso, se você aceitar o convite, será aplicado um questionário internacional de atividade física, assim como, um questionário específico para avaliar a sua qualidade de vida . Também faremos um teste de levantar-sentar da cadeira e depois um teste de força de mão e de coxa. Para avaliação da estrutura corporal será realizado a densitometria corporal total, que nada mais é do que um exame parecido com uma radiografia (Rx), mas com radiação menor, com duração de seis minutos, indolor e não usa nenhum contrate e nem medicamento. Á possibilidade de você sentir algum desconforto pela posição no equipamento (deitada) ou sensação de ansiedade e fobia, mas ressaltamos que são efeitos pouco prováveis e infrequentes, assim, este exame não apresenta risco para a saúde e nem risco de reação adversa, visto que não usa nenhum contraste nem medicamento. E por fim, será realizada uma coleta de sangue e de urina. A coleta de urina será arquivada em um ultrafreezer para posteriormente ser realizado a análise do perfil de metabólitos (metaboloma) por ressonância nuclear magnética (RNM).

Os possíveis riscos ou desconfortos decorrentes da participação na pesquisa são:a coleta de sangue poderá causar alguma dor, desconforto ou hematoma (mancha roxa) que deverá desaparecer em alguns dias. Além disso, poderá haver desconforto pelo tempo de resposta ao questionário, ou pelo conteúdo das perguntas, que envolvem aspectos de sua intimidade. Tanto a urina quanto o sangue coletado, serão armazenados paraque seja feito as análises necessárias. Esse material poderá permanecer armazenado e utilizado em até 3 anos. Também serão realizadas coletas de dados clínicos do seu prontuário eletrônico como: Idade, duração da doença (anos), presença de tabagismo atual, fator reumatóide, anticorpos anti-citrulinados de proteínas, erosões ao RX simples e tratamento farmacológico. Essa bateria de exames, questionários e avaliações levarão no máximo 3 horas. Todos os exames serão realizados no Hospital de Clínicas.

Os benefícios decorrentes da participação na pesquisa não serão diretos aos participantes, mas contribuirá para o aumento do conhecimento sobre o tema,

repercutindo na melhoria do manejo de futuros pacientes com a doença. Além disso, auxiliará na compreensão e ajudará a compreender o impacto do Lúpus eritematoso sistêmico na saúde funcional, esclarecendo o que muda no perfil funcional a longo prazo. Com isto, poderemos direcionar o tratamento e possibilitar o sucesso da terapia, bem como reduzir custos de medicações. Sua participação na pesquisa é totalmente voluntária, ou seja, não é obrigatória. Caso você decida não participar, ou ainda, desistir de participar e retirar seu consentimento, não haverá nenhum prejuízo ao atendimento que você recebe ou possa vir a receber na instituição. Não está previsto nenhum tipo de pagamento pela sua participação na pesquisa e você não terá nenhum custo com respeito aos procedimentos envolvidos. Caso ocorra alguma intercorrência ou dano, resultante de sua participação na pesquisa, você receberá todo o atendimento necessário, sem nenhum custo pessoal. Os dados coletados durante a pesquisa serão sempre tratados confidencialmente. Os resultados serão apresentados de forma conjunta, sem a identificação dos participantes, ou seja, o seu nome não aparecerá na publicação dos resultados.

Caso você tenha dúvidas, poderá entrar em contato com o pesquisador responsável Prof. Dr. Odirlei André Monticielo, pelo telefone (51) 3359 8340 ou com o Comitê de Ética em Pesquisa do Hospital de Clínicas de Porto Alegre (HCPA), pelo telefone (51) 33597640, ou no 2º andar do HCPA, sala 2229, de segunda à sexta, das 8h às 17h.

_____

Nome do participante da pesquisa

_____

Assinatura

_____

Nome do pesquisador que aplicou o Termo

_____

Assinatura

Local e Data: _____

ANEXO II

Critérios SLICC para classificação diagnóstica do lúpus eritematoso sistêmico

CRITÉRIOS CLÍNICOS	
1. Lúpus cutâneo agudo	Eritema malar, lúpus bolhoso, variante com necrose epidérmica tóxica, eritema maculopapular, eritema fotossensível (na ausência de dermatomiosite) **OU** lúpus cutâneo subagudo
2. Lúpus cutâneo crônico	Eritema discoide, lúpus hipertrófico (verrucoso), paniculite (lúpus *profundus*), lúpus eritematoso *tumidus*, eritema pérnio **OU** sobreposição de lúpus discoide e líquen plano
3. Alopecia não cicatricial	Afinamento difuso ou fragilidade capilar com quebra visível de cabelos (na ausência de outras causas
4. Úlceras orais ou nasais	Palato, boca e língua **OU** úlceras nasais, na ausência de outras causas
5. Alterações articulares	Sinovite em duas ou mais articulações, com edema ou derrame articular **OU** artralgia em duas ou mais articulações e rigidez matinal maior que 30 minutos
6. Serosites	Dor pleurítica típica por mais de um dia ou derrame pleural ou atrito pleural **OU** dor pericárdica típica por mais de um dia ou derrame pericárdico ou atrito pericárdico ou eletrocardiograma com sinais de pericardite, na ausência de outras causas
7. Alterações renais	Relação entre proteína e creatinina urinárias (ou proteinúria de 24 horas) com mais de 500 mg de proteínas nas 24 horas **OU** cilindros hemáticos
8. Alterações neurológicas	Convulsão, psicose, mononeurite múltipla, mielite, neuropatia periférica ou craniana **OU** estado confusional agudo
9. Anemia hemolítica	Presença de anemia hemolítica
10. Leucopenia ou linfopenia	Leucopenia $< 4.000/mm^3$ ou linfopenia $< 1.000/mm^3$, em pelo menos uma ocasião, na ausência de outras causas conhecidas
11. Trombocitopenia	Trombocitopenia $< 100.000/mm^3$ em pelo menos uma ocasião, na ausência de outras causas conhecidas
CRITÉRIOS IMUNOLÓGICOS	
1. Fator antinuclear	Fator antinuclear acima do valor de referência
2. Anti-DNAds	Anti-DNAds acima do valor de referência ou 2 vezes acima do valor de referência quando testado por ELISA
3. Anti-SM	Anticorpo anti-SM positivo
4. Antifosfolipídios	Anticoagulante lúpico positivo; VDRL falso-positivo; anticardiolipinas (IgA, IgG ou IgM) em títulos moderados ou altos; anti-beta 2-glicoproteína I (IgA, IgG ou IgM) positiva
5. Complementos reduzidos	Frações C3, C4 ou CH50
6. Coombs direto	Coombs direto positivo na ausência de anemia hemolítica

SLICC: Systemic Lupus International Collaborating Clinics; Anti-DNAds: anti-DNA dupla hélice; ELISA: enzyme-linked immunosorbent assay; Anti-SM: anticorpo anti-Smith. Adaptado de Petri et al (3)

ANEXO III

The systemic lupus international collaborating clinics/american college of rheumatology damage index (slicc/acr damage index)

Nome:

Prontuário: **Data**:

(Dano ocorrido desde o diagnóstico de LES determinado pela avaliação clínica e presente por pelo menos 6 meses. Episódios repetidos necessitam pelo menos de 6 meses de intervalo entre eles e devem ser pontuados como 2. A mesma lesão não pode ser pontuada 2 vezes)

ITEM	ESCORE (circular)
OCULAR (qualquer olho, por avaliação clínica)	
Catarata	0 1
Retinopatia ou atrofia óptica	0 1
NEUROPSIQUIÁTRICO	
Déficit cognitivo (déficit de memória, dificuldades com cálculos, pouca concentração, dificuldade de falar ou de escrever) **OU** psicose maior	0 1
Convulsões (necessitando tratamento por 6 meses)	0 1
AVC em qualquer época (se > 1 escore 2)	0 1 2
Neuropatia craniana ou periférica (exclui óptica)	0 1
Mielite transversa	0 1
RENAL	
DCE estimada ou medida < 50%	0 1
Proteinúria >3,5g/ 24 h **OU** Doença renal em estágio final (independente se diálise ou transplante)	0 1 3
PULMONAR	
Hipertensão pulmonar (ventrículo direito proeminente ou B2 hiperfonética)	0 1
Fibrose pulmonar (clínico e radiográfico)	0 1
Pulmão encolhido (Rx)	0 1
Fibrose pleural (Rx)	0 1
Infarto pulmonar (Rx) ou ressecção exceto por malignidade	0 1
CARDIOVASCULAR	
Angina **OU** bypass arterial coronariano	0 1
IAM em qualquer época (se > 1 escore 2)	0 1 2
Cardiomiopatia (disfunção ventricular)	0 1
Doença valvular (sopros >3+/6+)	0 1
Pericardite por 6 meses ou pericardiectomia	0 1
DOENÇA VASCULAR PERIFÉRICA	
Claudicação por 6 meses	0 1
Perda menor de tecido (polpas digitais)	0 1
Perda significante de tecido (dedo ou membro) (se > 1 escore 2)	0 1 2
Trombose venosa com ulceração, edema **OU** estase venosa	0 1
GASTROINTESTINAL	

Infarto ou ressecção do intestino (abaixo do duodeno), fígado, baço ou VB em qualquer ocasião (se > 1sítio, escore 2)	0	1	2
Insuficiência mesentérica	0	1	
Peritonite crônica	0	1	
Constrição **OU** cirurgia TGI superior em qualquer ocasião	0	1	
Insuficiência pancreática exigindo reposição enzimática ou com pseudocisto	0	1	
MUSCULOESQUELÉTICO			
Atrofia ou fraqueza muscular	0	1	
Artrite deformante ou erosiva (incluindo deformidades redutíveis e excluindo necrose avascular)	0	1	
Osteoporose com fratura ou colapso vertebral (excluindo necrose avascular)	0	1	
Necrose avascular (se > 1 escore 2)	0	1	2
Osteomielite	0	1	
Ruptura de tendão	0	1	
PELE			
Alopecia crônica cicatricial	0	1	
Extensa cicatrização ou panículo (exceto em couro cabeludo ou polpa digital)	0	1	
Ulceração cutânea (excluindo trombose) por período maior que 6 meses	0	1	
INSUFICÊNCIA GONADAL PREMATURA	0	1	
DIABETES (independente do tratamento)	0	1	
MALIGNIDADE (exceto displasia) (se > 1 sítio, escore 2)	0	1	2

TOTAL:_____ Arthritis & Rheumatism. 1997;40(5): 809-13

ANEXO IV

***The Systemic Lupus Erythematosus Disease Activity Index 2000*" (SLEDAI-2K)**

Escore	Item
8	Convulsão – início recente. Excluir outras causas, tais como distúrbios metabólicos, infecções ou medicamentos.
8	Psicose – distúrbio na percepção da realidade, incluindo alucinações, delírios, incoerências, perda de associações, pensamento não lógico, comportamento bizarro, desorganizado ou catatônico. Excluir outras causas, tais como uremia ou medicações
8	Síndrome cerebral orgânica – alteração da função mental, com prejuízo na orientação, memória ou outras funções intelectuais, com rápido surgimento e flutuações, incapacidade de sustentar a atenção, somado a pelo menos dois dos seguintes achados: distúrbio da percepção, diálogo incoerente, insônia, sonolência e aumento ou diminuição da atividade psicomotora. Excluir outras causas, tais como distúrbios metabólicos, infecções ou medicamentos
8	Visual – alterações no fundo do olho, como corpos citoides, hemorragias retinianas, exsudatos ou hemorragias na coroide ou nervo óptico. Excluir outras causas, tais como hipertensão, infecções ou medicamentos.
8	Nervos cranianos – surgimento de neuropatia sensitiva ou motora dos nervos cranianos.
8	Cefaleia lúpica – persistente e grave, enxaquecosa, com pouca resposta a analgésicos opioides.
8	AVC – evento de início recente e não relacionado com aterosclerose ou hipertensão.
8	Vasculite – ulceração, gangrena, nódulo, infarto periungueal, hemorragias puntiformes, biópsia ou arteriografia compatíveis com vasculite.
4	Artrite – duas articulações ou mais com sinais flogísticos.
4	Miosite – fraqueza ou dor muscular proximal com elevação de creatinofosfoquinase ou aldolase, ou eletroneuromiografia compatível com miosite ou biópsia com infiltrado inflamatório em fibra muscular.
4	Cilindros – hemáticos ou granulosos.
4	Hematúria – mais de 5 hemácias/campo de grande aumento. Excluir cálculos, infecções ou outras causas.
4	Proteinúria – acima de 0,5 g/24h.
4	Piúria – mais de 5 leucócitos/campo de grande aumento. Excluir infecção.
2	Eritema malar novo.
2	Alopecia – perda de cabelo anormal, difusa ou localizada.
2	Membranas mucosas – ulcerações nasais ou orais.
2	Pleurite – dor pleurítica com atrito pleural, ou derrame pleural ou espessamento pleural.
2	Pericardite – dor compatível com pericardite somada a pelo um dos seguintes achados: atrito pericárdico, derrame pericárdico, eletrocardiograma ou ecocardiograma compatíveis com pericardite.
2	Baixos complementos – diminuição do CH50, C3 ou C4 abaixo do limite da normalidade, de acordo com os valores de referência do exame.
2	Anti-DNA nativo – aumento acima do valor considerado normal para este exame.
1	Febre (temperatura axilar acima de 38º C).Excluir infecções.
1	Trombocitopenia (menos de 100.000 plaquetas/mm^3). Excluir outras causa, tais como medicamentos.

1	Leucopenia (menos de 3.000 leucócitos/mm^3). Excluir outras causas, tais como medicamentos.
TOTAL	

ANEXO V

Questionário de Qualidade de Vida em Lúpus Eritematoso Sistêmico (SLEQoL)

Obrigado por completar este questionário. Ele nos permitirá saber mais dos problemas do dia- a - dia que afetam os pacientes com lúpus. Também irá nos ajudar a entendê-los melhor e talvez conseguir melhorar o tratamento da doença. Para cada item, circule apenas um número que melhor demonstre o efeito/importância na sua vida. Por favor, não peça ajuda para responder estas questões, porque você é a melhor pessoa para saber da sua doença e como ela a afeta. Não existem respostas certas ou erradas.

FISICO

Por favor, use essa escala para responder às questões:

1 - sem dificuldade alguma;

2 - quase nada difícil;

3 - um pouco difícil;

4 - moderadamente difícil;

5 - difícil;

6 - muito difícil;

7 - extremamente difícil

1 Caminhar ao ar livre em ambiente plano. 1 2 3 4 5 6 7Fazer compras em lojas 1 2 3 4 5 6 7

2 Fechar e abrir torneiras. 1 2 3 4 5 6 7

3 Ir ao mercado/mercearia. 1 2 3 4 5 6 7

4 Tomar banho e enxugar-se. 1 2 3 4 5 6 7

5 Fazer 01 hora de caminhada. 1 2 3 4 5 6 7

Por favor, use essa escala para responder às próximas questões:

1 - de forma alguma;

2 - incomoda quase nada;

3 - incomoda um pouco;

4 - incomoda moderadamente;

5 - incomoda razoavelmente;

6 - incomoda muito;

7 - incomoda extremamente

ATIVIDADES

Na semana passada, a sua doença o incomodou em alguma destas atividades sociais ou de trabalho?

7 No trabalho ou nas atividades escolares. 1 2 3 4 5 6 7

8 Na carreira ou educação. 1 2 3 4 5 6 7

9 Nas ausências no trabalho ou na escola. 1 2 3 4 5 6 7

10 No relacionamento com amigos ou familiares 1 2 3 4 5 6 7

11 Na prática de exercícios físicos. 1 2 3 4 5 6 7

12 Nas atividades sexuais 1 2 3 4 5 6 7

13 Na participação em atividades de lazer e divertimento 1 2 3 4 5 6 7

14 Não conseguir sair em dia com sol forte 1 2 3 4 5 6 7

15 Ganhar menos dinheiro porque tem lúpus 1 2 3 4 5 6 7

SINTOMAS

Na semana passada, por causa do seu lúpus, estes sintomas o incomodaram?

16 Esquecimento (memória fraca). 1 2 3 4 5 6 7

17 Perda de apetite. 1 2 3 4 5 6 7

18 Cansaço. 1 2 3 4 5 6 7

19 Dificuldade de prestar atenção (de concentração 1 2 3 4 5 6 7

20 Coceira. 1 2 3 4 5 6 7

21 Feridas na boca. 1 2 3 4 5 6 7

22 Feridas, dor ou formigamento na pele. 1 2 3 4 5 6 7

23 Dor ou inchaço nas juntas 1 2 3 4 5 6 7

Por favor, use essa escala para responder às próximas questões:

1 - de forma alguma;

2 - incomoda quase nada;

3 - incomoda um pouco;

4 - incomoda moderadamente;

5 - incomoda razoavelmente;

6 - incomoda muito;

7 - incomoda extremamente

TRATAMENTO

24 Medo de agulhas. 1 2 3 4 5 6 7

25 Evitar alguma comida por causa da doença. 1 2 3 4 5 6 7

26 Usar remédios todos os dias 1 2 3 4 5 6 7

27 Vir ao hospital ou clínica. 1 2 3 4 5 6 7

Por favor use essa escala para responder as próximas questões:

1 - de forma alguma;

2 - quase nunca;

3 - um pouco frequente;

4 - moderadamente frequente;

5 - razoavelmente frequente;

6 - muito frequente;

7 - extremamente frequente

HUMOR

Com que frequência , durante a semana passada, você se incomodou com as seguintes emoções, por causa do seu lúpus?

28 Sentiu-se diferente das outras pessoas 1 2 3 4 5 6 7

29 Sentiu-se triste. 1 2 3 4 5 6 7

30 Sentiu depressão (tristeza profunda). 1 2 3 4 5 6 7

31 Sentiu ansiedade (apreensiva com o que possa acontecer 1 2 3 4 5 6 7

AUTO -IMAGEM

Com que frequência, na semana passada ,você se incomodou pelos seguintes sentimentos como

consequência do seu lúpus?

32 Desejo de que as pessoas não soubessem que tenho lúpus 1 2 3 4 5 6 7

33 Amigos e colegas fizerem chacotas ou pilhérias comigo 1 2 3 4 5 6 7

34 Me senti inferior aos outros 1 2 3 4 5 6 7

35 Senti vergonha do meu lúpus. 1 2 3 4 5 6 7

36. Preocupação quanto aos gastos de dinheiro na família por minha causa1 2 3 4 5 6 7

37 Preocupação quanto a não eficácia dos remédios. 1 2 3 4 5 6 7

38 Preocupação quanto aos efeitos colaterais dos remédios 1 2 3 4 5 6 7

39 Medo de receber más notícias dos médicos. 1 2 3 4 5 6 7

40 Consumo maior de bebidas alcoólicas ou fumo. 1 2 3 4 5 6 7

ANEXO VI

IPAQ- Versão curta

AGORA FALAREMOS SOBRE ATIVIDADES FÍSICAS.

Para responder às questões, lembramos que:

► atividades físicas VIGOROSAS, são aquelas que precisam de um grande esforço físico e que fazem respirar MUITO mais forte que o normal.

► atividades físicas MODERADAS, são aquelas que precisam de algum esforço físico e que fazem respirar UM POUCO mais forte que o normal.

1A) Desde o dia (*x da semana passada)* quantos dias o(a) sr.(a) caminhou por mais de 10 minutos seguidos? Pense nas caminhadas no trabalho, em casa, como forma de transporte para ir de um lugar ao outro, por lazer, por prazer ou como forma de exercício que duraram mais de 10 minutos seguidos.

(0) nenhum → *pule para a questão 2*

dias _____por semana.

1b) nos dias em que o (a) sr.(a) caminhou, quanto tempo, no total, o(a) sr.(a) caminhou por dia?

_____horas _____minutos p/ dia

AGORA PENSE EM OUTRAS ATIVIDADES FÍSICAS FORA A CAMINHADA.

2A. Em quantos dias da última semana, você realizou atividades **MODERADAS** por pelo menos 10 minutos contínuos, como por exemplo, pedalar leve na bicicleta, nadar, dançar, fazer ginástica aeróbica leve, jogar vôlei recreativo, carregar pesos leves, fazer serviços domésticos na casa, no quintal ou no jardim como varrer, aspirar, cuidar do jardim, ou qualquer atividade que fez aumentar **moderadamente** sua respiração ou batimentos do coração **(POR FAVOR NÃO INCLUA CAMINHADA)**

dias_____por **SEMANA** ( ) Nenhum

2b. Nos dias em que você fez essas atividades moderadas por pelo menos 10 minutos contínuos, quanto tempo no total você gastou fazendo essas atividades **por dia**?

horas:_____Minutos: _____

3A. Em quantos dias da última semana, você realizou atividades **VIGOROSAS** por pelo menos 10 minutos contínuos, como por exemplo correr, fazer ginástica aeróbica, jogar futebol, pedalar rápido na bicicleta, jogar basquete, fazer serviços domésticos pesados em casa, no quintal ou cavoucar no jardim, carregar pesos elevados ou qualquer atividade que fez aumentar **MUITO** sua respiração ou batimentos do coração.

dias____por **SEMANA** ( ) Nenhum

3B. Nos dias em que você fez essas atividades vigorosas por pelo menos 10 minutos contínuos quanto tempo no total você gastou fazendo essas atividades **por dia**?

horas:_____Minutos: _____

Estas últimas questões são sobre o tempo que você permanece sentado diariamente, no trabalho, na escola ou faculdade, em casa e durante seu tempo livre. Estas questões incluem o tempo sentado estudando, sentado enquanto descansa, fazendo lição de casa, visitando um amigo, lendo, sentado ou deitado assistindo TV.

4a. Quanto tempo no total você gasta sentado durante um **dia de semana**?

_____horas_____minutos

4b. Quanto tempo no total você gasta sentado durante um **dia de final de semana**?

_____horas_____minutos

ANEXO VII

Fluxograma para as coletas e dados

Nome: Prontuário:

ID: Data:

PROCEDIMENTOS	**SITUAÇÃO**
TCLE	
COLETA DE SANGUE	
COLETA DE URINA	
DXA	
ULTRASSONOGRAFIA	
IPAQ	
SARC-F	
PANTURRILHA	
SLEQoL	
SLEDAI	
HANDGRIP	**D** 1ª MEDIDA: 2ª MEDIDA: 3ª MEDIDA: **E** 1ª MEDIDA: 2ª MEDIDA: 3ª MEDIDA:
TUG	1ª MEDIDA: 2ª MEDIDA:
SPPB	1ª - 1B - 1C - 2ª - 2B - C - TOTAL
SENTAR / LEVANTAR-SE (30 seg)	