

UNIVERSIDADE FEDERAL DE UBERLÂNDIA
FACULDADE DE MEDICINA
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE

ASSOCIAÇÃO DOS ÁCIDOS GRAXOS SATURADOS NO PLASMA
COM ÍNDICE DE MASSA MUSCULAR ESQUELÉTICA
APENDICULAR E FORÇA EM NORTE-AMERICANOS (NHANES 2011-
2012)

HEITOR OLIVEIRA SANTOS

UBERLÂNDIA - MG
2023

HEITOR OLIVEIRA SANTOS

**ASSOCIAÇÃO DOS ÁCIDOS GRAXOS SATURADOS NO PLASMA
COM ÍNDICE DE MASSA MUSCULAR ESQUELÉTICA
APENDICULAR E FORÇA EM NORTE-AMERICANOS (NHANES 2011-
2012)**

**Tese apresentada ao Programa de
Pós-Graduação em Ciências da
Saúde da Faculdade de Medicina da
Universidade Federal de Uberlândia,
como requisito parcial para a
obtenção do título de Doutor em
Ciências da Saúde.**

**Área de concentração: Ciências da
Saúde.**

**Orientador: Prof. Dr. Erick Prado
de Oliveira**

UBERLÂNDIA - MG

2023

Ficha Catalográfica Online do Sistema de Bibliotecas da UFU
com dados informados pelo(a) próprio(a) autor(a).

S237 2023	Santos, Heitor Oliveira, 1995- ASSOCIAÇÃO DOS ÁCIDOS GRAXOS SATURADOS NO PLASMA COM ÍNDICE DE MASSA MUSCULAR ESQUELÉTICA APENDICULAR E FORÇA EM NORTE-AMERICANOS (NHANES 2011-2012) [recurso eletrônico] : Gordura saturada plasmática e parâmetros musculares / Heitor Oliveira Santos. - 2023. Orientador: Erick Prado de Oliveira. Tese (Doutorado) - Universidade Federal de Uberlândia, Pós-graduação em Ciências da Saúde. Modo de acesso: Internet. Disponível em: http://doi.org/10.14393/ufu.te.2023.557 Inclui bibliografia. 1. Ciências médicas. I. Oliveira, Erick Prado de, 1983-, (Orient.). II. Universidade Federal de Uberlândia. Pós-graduação em Ciências da Saúde. III. Título. CDU: 61
--------------	---



UNIVERSIDADE FEDERAL DE UBERLÂNDIA
 Coordenação do Programa de Pós-Graduação em Ciências da Saúde
 Av. Pará, 1720, Bloco 2H, Sala 11 - Bairro Umuarama, Uberlândia-MG, CEP 38400-902
 Telefone: (34) 3225-8628 - www.ppcs.famed.ufu.br - ppcs@famed.ufu.br



ATA DE DEFESA - PÓS-GRADUAÇÃO

Programa de Pós-Graduação em:	Ciências da Saúde				
Defesa de:	Tese de Doutorado Nº 11/PPCSA				
Data:	16.10.2023	Hora de início:	13:00h	Hora de encerramento:	17:00h
Matrícula do Discente:	12113CSD007				
Nome do Discente:	Heitor Oliveira Santos				
Título do Trabalho:	ASSOCIAÇÃO DOS ÁCIDOS GRAXOS SATURADOS NO PLASMA COM ÍNDICE DE MASSA MUSCULAR ESQUELÉTICA APENDICULAR E FORÇA EM NORTE-AMERICANOS (NHANES 2011- 2012)				
Área de concentração:	Ciências da Saúde				
Linha de pesquisa:	2 - DIAGNÓSTICO, TRATAMENTO E PROGNÓSTICO DAS DOENÇAS E AGRAVOS À SAÚDE				
Projeto de Pesquisa de vinculação:	NUTRIÇÃO E EXERCÍCIO FÍSICO APLICADOS À SAÚDE E DESEMPENHO HUMANO				

Reuniu-se em web conferência pela plataforma Zoom, em conformidade com a PORTARIA Nº 36, DE 19 DE MARÇO DE 2020 da COORDENAÇÃO DE APERFEIÇOAMENTO DE PESSOAL DE NÍVEL SUPERIOR - CAPES, pela Universidade Federal de Uberlândia, a Banca Examinadora, designada pelo Colegiado do Programa de Pós-graduação em Ciências da Saúde, assim composta: Profs. Drs. Gederson Kardec Gomes (IMECAP), Rodrigo Cauduro Oliveira Macedo (UNISC), Ana Elisa Rinaldi (UFU), Yara Cristina de Paiva Maia (UFU) e Erick Prado de Oliveira (UFU), orientador do candidato.

Iniciando os trabalhos, o presidente da mesa, Prof. Dr. Erick Prado de Oliveira, apresentou a Comissão Examinadora e o candidato, agradeceu a presença do público, e concedeu ao Discente a palavra para a exposição do seu trabalho. A duração da apresentação do Discente e o tempo de arguição e resposta foram conforme as normas do Programa.

A seguir o senhor(a) presidente concedeu a palavra, pela ordem sucessivamente, aos(às) examinadores(as), que passaram a arguir o(a) candidato(a). Ultimada a arguição, que se desenvolveu dentro dos termos regimentais, a Banca, em sessão secreta, atribuiu o resultado final, considerando o(a) candidato(a):

Aprovado.

Esta defesa faz parte dos requisitos necessários à obtenção do título de Doutor.

O competente diploma será expedido após cumprimento dos demais requisitos, conforme as normas do Programa, a legislação pertinente e a regulamentação interna da UFU.

Nada mais havendo a tratar foram encerrados os trabalhos. Foi lavrada a presente ata que após lida e achada conforme foi assinada pela Banca Examinadora.



Documento assinado eletronicamente por **Gederson Kardec Gomes, Usuário Externo**, em 16/10/2023, às 17:26, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do [Decreto nº 8.539, de 8 de outubro de 2015](#).



Documento assinado eletronicamente por **Ana Elisa Madalena Rinaldi, Professor(a) do Magistério Superior**, em 16/10/2023, às 17:35, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do [Decreto nº 8.539, de 8 de outubro de 2015](#).



Documento assinado eletronicamente por **Erick Prado de Oliveira, Professor(a) do Magistério Superior**, em 16/10/2023, às 17:36, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do [Decreto nº 8.539, de 8 de outubro de 2015](#).



Documento assinado eletronicamente por **Rodrigo Cauduro Oliveira Macedo, Usuário Externo**, em 16/10/2023, às 17:36, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do [Decreto nº 8.539, de 8 de outubro de 2015](#).



Documento assinado eletronicamente por **Yara Cristina de Paiva Maia, Professor(a) do Magistério Superior**, em 16/10/2023, às 17:36, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do [Decreto nº 8.539, de 8 de outubro de 2015](#).



A autenticidade deste documento pode ser conferida no site https://www.sei.ufu.br/sei/controlador_externo.php?acao=documento_conferir&id_orgao_acesso_externo=0, informando o código verificador **4890824** e o código CRC **4B93B356**.

FOLHA DE APROVAÇÃO

Heitor Oliveira Santos.

Associação dos ácidos graxos saturados no plasma com índice de massa muscular esquelética apendicular e força em norte-americanos (NHANES 2011-2012)

Presidente da banca: Prof. Dr. Erick Prado de Oliveira

Tese apresentada ao Programa de Pós-Graduação em Ciências da Saúde da Faculdade de Medicina da Universidade Federal de Uberlândia, como requisito parcial para a obtenção do título de Doutor em Ciências da Saúde.

Área de concentração: Ciências da Saúde.

Orientador: Prof. Dr. Erick Prado de Oliveira.

Banca Examinadora

Titular: Prof^ª. Dr^ª. Yara Cristina Paiva Maia

Instituição: Universidade Federal de Uberlândia/MG

Titular: Prof^ª. Dr^ª. Ana Elisa Madalena Rinaldi

Instituição: Universidade Federal de Uberlândia/MG

Titular: Prof. Dr. Gederson Kardec Gomes

Instituição: IMEPAC (Instituto Master de Ensino Presidente Antônio Carlos),
Araguari/MG

Titular: Prof^ª. Dr. Rodrigo Cauduro Oliveira Macedo

Universidade de Santa Cruz do Sul (UNISC)/RS

DEDICATÓRIA

À minha família, em especial à minha mãe, meu irmão e meu padrasto, pessoas que convívio diariamente.

À minha avó materna, por todo cuidado durante a minha infância.

À minha escola de formação, colégio Marista Champagnat de Uberlândia, por ter me educado desde o Ensino Infantil até o Ensino Médio. Em especial, à diretora Silvania Pereira da Costa e à coordenadora Cissa Sousa.

Ao meu pai (*in memoriam*), por ter sido um pai presente na minha vida, meu maior exemplo de simpatia, agradando e tendo o reconhecimento de inúmeras pessoas. Serei muito feliz se um dia for um pai à altura dele.

À minha tia Thelma (*in memoriam*), por ter sido uma tia presente na minha vida, a felicidade e humildade em pessoa.

AGRADECIMENTOS

Ao prof. Dr. Erick Prado de Oliveira, pela orientação e amplo ensinamento científico, da graduação ao doutorado. Sem dúvidas, é um líder exemplar, gerenciando um grande grupo de pesquisa (LaNES), dando oportunidades no desenvolvimento da oratória e na escrita científica, fatores cruciais no sucesso de um docente.

À minha família, em especial, mãe, irmão e padrasto.

Aos membros do grupo LaNES, em especial aqueles que foram coautores dos dois artigos do meu doutorado: Rafaela, Larissa, Flávia, Maria Eduarda e Breno.

À banca examinadora: professores/professoras Yara, Ana Elisa, Nilson, Gederson, Rodrigo e Cinthia. Aprendi com todos, em vários momentos da minha vida acadêmica. Cada um tem uma característica única, tanto como profissionais e, sobretudo, como pessoas.

Ao programa de Pós-Graduação em Ciências da Saúde como um todo, especialmente pela bolsa concedida, a qual me permitiu grande dedicação ao doutorado.

Às secretárias do programa, Viviane Pires e Gisele de Melo Rodrigues, principalmente na reta final.

Meu sincero agradecimento a todos.

*“Faça o teu melhor, na condição
que você tem, enquanto você não
tem condições melhores, para fazer
melhor ainda!”*

Mario Sergio Cortella

RESUMO

Introdução: O potencial pró-inflamatório dos ácidos graxos saturados (AGS) pode prejudicar o músculo esquelético e, portanto, seus parâmetros relacionados. Algumas pesquisas investigaram a associação entre AGS dietéticos e parâmetros musculares, mas pouco se sabe sobre os níveis plasmáticos de AGS neste cenário. **Objetivos:** Verificar a associação entre os níveis plasmáticos de AGS e parâmetros musculares (massa magra e força muscular) em adultos e idosos.

Métodos: Uma pesquisa transversal foi realizada utilizando dados do *National Health and Nutrition Examination Survey* (NHANES) 2011-2012, dos quais, 937 indivíduos com idade entre 20 e 59 anos e 1591 com idade entre 20 e 80 anos foram incluídos para analisar a massa magra e força muscular, respectivamente. Cromatografia gasosa-espectrometria de massa foi utilizada para detectar os AGS totais no plasma e seus subtipos. A massa magra foi avaliada através do índice de massa magra apendicular (IMMA) por meio da divisão da massa magra apendicular pela estatura ao quadrado. A força muscular foi avaliada através do somatório da força de preensão manual. A análise de regressão linear foi realizada para avaliar as associações sob controle de potenciais fatores de confusão. **Resultados:** Os AGS totais plasmáticos e seus subtipos (ácido cáprico, ácido láurico, ácido mirístico, ácido palmítico, ácido esteárico, ácido margárico, ácido pentadecanóico, ácido araquídico, ácido tricosanóico, ácido lignocérico e ácido docosanóico) não se associaram com o IMMA (ajustes de ingestão de energia e proteínas, tabagismo, renda familiar, diabetes, hipertensão, álcool, estado civil, escolaridade, artrite, massa gorda, atividade física, idade, sexo e etnia). Igualmente, os AGS totais plasmáticos e seus subtipos não foram associados com a força de preensão manual (ajustes de ingestão de energia e proteínas, tabagismo, renda familiar, diabetes, hipertensão arterial, álcool, estado civil, escolaridade, artrite, atividade física, idade, sexo, raça e índice de massa corporal), entretanto, quando os indivíduos foram divididos de acordo com a idade, foram observadas associações negativas com o ácido cáprico ($\beta = -0,2978$; IC95% = -0,5855, -0,0100; $p = 0,043$) e ácido esteárico ($\beta = -0,0058$; IC95% = -0,0100, -0,0003; $p = 0,038$) apenas para aqueles com idade <60 anos. **Conclusão:** No geral, os AGS plasmáticos totais e seus subtipos não estão associados com o IMMA e força muscular em norte-americanos. Observou-se, apenas, associação inversa para força muscular com ácido esteárico e ácido cáprico para aqueles com idade <60 anos.

Palavras-chave: lipídios; massa muscular; força muscular; ácidos graxos saturados.

SUMMARY

Background: The pro-inflammatory potential of saturated fatty acids (SFAs) can hinder skeletal muscle and hence its related parameters. Some research has investigated the association between dietary SFAs and muscle parameters, but little is known about the plasma SFA levels in this regard. **Aims:** Thus, we aimed to verify the association between plasma SFA levels and muscle parameters (muscle mass and strength) in adults. **Methods:** A cross-sectional research was performed using the National Health and Nutrition Examination Survey (NHANES) 2011-2012, whereby 937 subjects aged 20-59 and 1591 aged 20-80 years were included for AMMI and muscle strength, respectively. Gas chromatography-mass spectrometry was used to detect plasma total SFAs and their subtypes. Muscle strength was assessed through the sum of handgrip strength. AMMI was calculated by dividing appendicular lean mass by height squared. Linear regression analysis was performed to evaluate the association between SFAs and AMMI adjusting for potential confounders. **Results:** No association (p -value > 0.05) was observed between plasma total SFAs and their subtypes (capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, margaric acid, pentadecanoic acid, arachidic acid, tricosanoic acid, lignoceric acid, and docosanoic acid) with AMMI (adjustments for energy and protein intakes, smoking, family income, diabetes, hypertension, alcohol, marital status, education level, arthritis, fat mass, physical activity, age, sex, and race). Plasma total SFAs and their individual types were not associated with handgrip strength (adjustments for energy intake, protein intake, smoking, family income, diabetes, arterial hypertension, alcohol, marital status, education level, arthritis, physical activity, age, sex, race, and body mass index), however, when subjects were divided according to age, negative associations were observed for capric acid (β -value = -0.2978; 95%CI = -0.5855, -0.0100; $p = 0.043$) and stearic acid (β -value = -0.0058; 95%CI = -0.0100, -0.0003; $p = 0.038$) levels only for those aged <60 years. **Conclusion:** Overall, plasma total SFAs and their types are not associated with AMMI and muscle strength in Americans. We only observed an inverse association for muscle strength with stearic acid and capric acid for those aged <60 years.

Keywords: lipids; muscle mass; muscle strength; saturated fatty acids.

LISTA DE ILUSTRAÇÕES

Artigo 1 (Plasma saturated fatty acids are not associated with appendicular skeletal muscle mass index in adults: NHANES 2011-2012)

Figure 1. Flowchart of the subjects evaluated. Sample selection from NHANES, 2011-2012.....47

Artigo 2 (Association between plasma saturated fatty acids and muscle strength in Americans aged <60 versus ≥60 years: Results from NHANES 2011-2012)

Figure 1. Flowchart of the sample selection from NHANES (2011-2012).....74

LISTA DE TABELAS

Artigo 1 (Plasma saturated fatty acids are not associated with appendicular skeletal muscle mass index in adults: NHANES 2011-2012)

Table 1. Sociodemographic, body composition, anthropometric, and dietary characteristics the in total sample and according to plasma total saturated fatty acids levels. Data from NHANES (2011-2012).....48

Table 2. Linear regression between appendicular muscle mass index with plasma total SFAs and their individual types. Results from NHANES (2011-2012).....51

Table 3. Linear regression between AMMI and tertiles of plasma total SFAs and their individual types. Results from NHANES (2011-2012).....52

Artigo 2 (Association between plasma saturated fatty acids and muscle strength in Americans aged <60 versus ≥60 years: Results from NHANES 2011-2012)

Table 1. Sociodemographic, anthropometric, and dietary characteristics the in total sample and according to age. Data from NHANES (2011-2012).....75

Table 2. Linear regression between muscle strength with plasma total SFAs and their individual types in all patients regardless of age. Results from NHANES (2011-2012).....78

Table 3. Linear regression between muscle strength with plasma total SFAs and their individual types according to age (<60 years and ≥60 years). Results from NHANES (2011-2012).....79

LISTA DE ABREVIATURAS E SÍMBOLOS

Lista Geral

AGS: ácidos graxos saturados

DXA: absormetria de raios-x de dupla energia (DXA)

IMMA: índice de massa magra apendicular

FPM: força de pressão manual

Lista dos Artigos

AMMI: Appendicular muscle mass index

BMI: Body mass index

CDC: Centers for Disease Control and Prevention

CI: confidence intervals

DXA: Dual-energy x-ray absorptiometry

FNDSS: Nutrient Database for Dietary Studies

HGS: Handgrip strength

SFAs: Saturated fatty acids

NCHS: National Center for Health Statistics

NHANES: National Health and Nutrition Examination

mmol/L: millimoles per liter

*: Statistical significance

β : Regression coefficient

Considerações iniciais

A formatação desta tese segue o modelo alternativo estabelecido pelo Programa de Pós-Graduação e Pesquisa em Ciências Saúde da Faculdade de Medicina da Universidade Federal de Uberlândia, o qual determina que os resultados da tese sejam apresentados em formato de artigos científicos.

A tese foi organizada nas seguintes seções: inicialmente, uma Fundamentação Teórica será apresentada como forma de revisão da literatura sobre os temas abordados na tese. Serão então elencados os Objetivos em que são expostos os propósitos do estudo; os Resultados, que contemplam dois artigos elaborados; a Conclusão, que discorre sobre a síntese dos principais resultados do estudo; as Perspectivas, nas quais são apresentadas as expectativas para estudos futuros; e o Pós-texto, no qual estão incluídos referências bibliográficas, anexos e apêndices.

Ambos os artigos foram adaptados à norma do periódico Clinical Nutrition (Fator de impacto = 6,360).

Sumário

1. INTRODUÇÃO.....	17
2. FUNDAMENTAÇÃO TEÓRICA	19
2.1. <i>Declínio da massa e força muscular no envelhecimento.....</i>	19
2.2. <i>Relação entre nutrientes e grupos alimentares com massa e força muscular.....</i>	19
2.3. <i>Mecanismos inflamatórios dos ácidos graxos saturados no miócito</i>	21
2.4. <i>Índice de massa magra apendicular.....</i>	22
2.5. <i>Força de preensão manual</i>	23
2.6. <i>Consumo de ácidos graxos saturados e índice de massa magra apendicular.....</i>	24
2.7. <i>Consumo de ácidos graxos saturados e força de preensão manual</i>	24
2.8. <i>Concentrações plasmáticas de ácidos graxos saturados e parâmetros musculares.....</i>	25
2.9. <i>População americana.....</i>	26
3. OBJETIVOS.....	27
3.1. <i>Objetivo geral</i>	27
3.2. <i>Objetivos específicos.....</i>	28
4. ARTIGOS	29
4.1. Artigo 1 (Plasma saturated fatty acids are not associated with appendicular skeletal muscle mass index in adults: NHANES 2011-2012).....	29
4.2. Artigo 2 (Association between plasma saturated fatty acids and muscle strength in Americans aged <60 versus ≥60 years: Results from NHANES 2011-2012).....	53
5. CONCLUSÃO	80
6. PERSPECTIVAS	80
7. PÓS-TEXTO – REFERÊNCIAS.....	81

1. INTRODUÇÃO

A preservação da massa e força muscular é fundamental no envelhecimento saudável (SEIDEL; BRAYNE; JAGGER, 2011). Como indicadores cruciais de saúde, a massa e força muscular estão associadas com maior qualidade de vida por melhorar a prática das atividades físicas diárias e reduzir o risco de inúmeras doenças crônicas não-transmissíveis (doenças cardiovasculares, doenças ortopédicas, diabetes, câncer etc.) e mortalidade (ABRAMOWITZ; HALL; AMODU; SHARMA *et al.*, 2018; BOKSHAN; DEPASSE; DANIELS, 2016; HONG; CHANG; JUNG; YUN *et al.*, 2017; KIM; SHIN; LEE; SONG *et al.*, 2021; PSUTKA; BOORJIAN; MOYNAGH; SCHMIT *et al.*, 2016; SRIKANTHAN; HORWICH; CALFON PRESS; GORNBEIN *et al.*, 2021). Coletivamente, a redução da massa e força muscular pode preceder o desenvolvimento de doenças por serem, parcialmente, oriundas de um pior estado nutricional (HOUSTON; NICKLAS; DING; HARRIS *et al.*, 2008).

De forma mais específica, a fraqueza muscular mensurada pela força de pressão manual (FPM) está associada com resultados adversos graves, tais como morbidade, incapacidade, dependência e morte, conforme mostrado por pesquisas longitudinais envolvendo países de rendas e ambientes socioculturais variados (LEONG; TEO; RANGARAJAN; LOPEZ-JARAMILLO *et al.*, 2015). O índice de massa magra apendicular (IMMA) também está inversamente associado com mortalidade; contudo, esta associação não está completamente explicada por diferenças na FPM ou outros fatores clínicos e demográficos conhecidos (DE SANTANA; PREMAOR; TANIGAVA; PEREIRA, 2021).

Uma redução considerável do IMMA é um fator preditivo de mortalidade por todas as causas em homens idosos independentemente da idade (SZULC;

MUNOZ; MARCHAND; CHAPURLAT *et al.*, 2010). Esta associação inversa com a mortalidade é observada tanto em homens quanto em mulheres (LEE; GIOVANNUCCI, 2018). Representativamente, um IMMA elevado foi associado com uma redução de 18% (por 1 kg/m²) no risco de mortalidade em adultos norte-americanos utilizando dados do *National Health and Nutrition Examination Survey* (NHANES) (ABRAMOWITZ; HALL; AMODU; SHARMA *et al.*, 2018).

O alto consumo de ácidos graxos saturados (AGS) é um problema global, afetando principalmente norte-americanos (DANIEL; CROSS; KOEBNICK; SINHA, 2011; GREENBERG; BUIJSSE, 2013; YU; HU, 2018). Do ponto de vista bioquímico, o potencial pró-inflamatório dos AGS afeta as vias moleculares do miócito (LIPINA; HUNDAL, 2017), hipoteticamente, podendo culminar em menor hipertrofia e força muscular. Alguns estudos analisaram a associação do consumo de AGS com massa magra e força muscular (ARIAS-FERNÁNDEZ; STRUIJK; RODRÍGUEZ-ARTEALEJO; LOPEZ-GARCIA *et al.*, 2020; GEDMANTAITE; CELIS-MORALES; HO; PELL *et al.*, 2020; TATANGELO; MUOLLO; GHIOTTO; SCHENA *et al.*, 2022). Em contrapartida, pouco se sabe a respeito da associação da massa magra e força muscular com os AGS plasmáticos, os quais podem ser mais precisos que o consumo de AGS estimado por inquéritos alimentares devido subrelatos e dificuldade de determinação em receitas e alimentos (MACDIARMID; BLUNDELL, 1998; WATERWORTH; KERR; MCMANUS; COSTELLO *et al.*, 2022).

Portanto, investigar a associação dos AGS plasmáticos com o IMMA e a FPM como parâmetros pragmáticos relacionados à massa e força muscular é promissor. Os aspectos básicos destas variáveis são pormenorizados na

fundamentação teórica a seguir, a qual, também, ressalta a importância científica inerente às novidades.

2. FUNDAMENTAÇÃO TEÓRICA

2.1. Declínio da massa e força muscular no envelhecimento

Há um declínio da massa e força muscular em idosos devido à senescência e aos processos de inflamatórios e estresse oxidativo associados (WILKINSON; PIASECKI; ATHERTON, 2018). Estima-se uma redução de ~3,5-5,5 kg de massa muscular em homens e de ~3,0-3,5 kg em mulheres quando a faixa etária de adultos jovens (18-30 anos), respectivamente, após os 60 anos (HEYMSFIELD; STANLEY; PIETROBELLI; HEO, 2020; JANSSEN; HEYMSFIELD; WANG; ROSS, 2000). Ademais, enquanto o declínio na força muscular não é expressivo em adultos jovens e de meia-idade, ele é pronunciado em idosos, com uma perda estimada de 15% por década (TATANGELO; MUOLLO; GHIOTTO; SCHENA *et al.*, 2022).

2.2. Relação entre nutrientes e grupos alimentares com massa e força muscular

Vários nutrientes, tais como proteínas e vitaminas (principalmente as antioxidantes) vêm ganhando destaque fisiológico por aprimorar a função e a massa muscular (BEASLEY; SHIKANY; THOMSON, 2013; CESARI; PAHOR; BARTALI; CHERUBINI *et al.*, 2004). Além disso, o consumo de ácidos graxos insaturados (ácidos graxos monoinsaturados e poliinsaturados) também pode ser benéfico ao músculo esquelético devido à atividade anti-inflamatória, conforme suportado por ensaios clínicos randomizados e estudos longitudinais

abarcando idosos (isto é, uma população de maior risco de fragilidade) (RODACKI; RODACKI; PEREIRA; NALIWAIKO *et al.*, 2012; SANDOVAL-INSAUATI; PÉREZ-TASIGCHANA; LÓPEZ-GARCÍA; GARCÍA-ESQUINAS *et al.*, 2016; SMITH; JULLIAND; REEDS; SINACORE *et al.*, 2015). Entretanto, maior atenção é necessária concernente à atividade pró-inflamatória dos AGS com a massa e força muscular.

Além de uma visão exclusiva dos AGS, o consumo de determinados grupos alimentares deve ser observado para mimetizar a vida real. O consumo de embutidos e alimentos de padaria conhecidos por serem ricos em AGS foram associados com um risco aumentado de fraqueza muscular em indivíduos de meia idade e idosos (ARIAS-FERNÁNDEZ; STRUIJK; RODRÍGUEZ-ARTALEJO; LOPEZ-GARCIA *et al.*, 2020). Outrossim, um padrão alimentar rico em carne vermelha e manteiga foi associado com menor força muscular e desempenho físico em octogenários (>85 anos) acompanhados durante 5 anos (GRANIC; JAGGER; DAVIES; ADAMSON *et al.*, 2016).

Apesar destes dados de associação, vale salientar que o desenho clínico observacional não é o ideal para deduzir recomendações devido a fatores de confusão residuais intrínsecos ao estilo de vida. Portanto, deve-se ter senso crítico em alguns aspectos, já que o contexto alimentar do cotidiano é extremamente amplo. Por exemplo, embora o consumo de carne vermelha possa ser associado com menor força muscular por teoricamente ser rica em AGS (GRANIC; JAGGER; DAVIES; ADAMSON *et al.*, 2016), vários estudos mostram que o consumo de carne vermelha está associado com melhor status da massa magra e é endossado como uma das principais estratégias alimentares objetivando a hipertrofia (ASP; RICHARDSON; COLLENE; DROLL

et al., 2012; DALY; O'CONNELL; MUNDELL; GRIMES *et al.*, 2014; LYNCH; KOOPMAN, 2018). Esta contradição provavelmente existe pois o teor de AGS varia conforme o corte da carne, de modo que substâncias específicas de carnes processadas podem ser nocivas à saúde independentemente da quantidade dos AGS (CHAI; MORIMOTO; COONEY; FRANKE *et al.*, 2017).

2.3. Mecanismos inflamatórios dos ácidos graxos saturados no miócito

Os AGS podem afetar inúmeras vias moleculares devido ao estímulo pró-inflamatório sistêmico (FRITSCHÉ, 2015; HÅVERSEN; DANIELSSON; FOGELSTRAND; WIKLUND, 2009; HUANG; RUTKOWSKY; SNODGRASS; ONO-MOORE *et al.*, 2012). Este estímulo inflamatório é evidente no miócito, conforme mostrado *in vitro* e em roedores (PILLON; ARANE; BILAN; CHIU *et al.*, 2012; SEBE; TSUTSUMI; SENOURA; KISHI *et al.*, 2022).

O excesso de palmitato no miócito é o principal modelo biológico que representa o efeito deletério dos AGS em diversas vias moleculares em nível citosólico e nuclear, gerando ceramidas e ativando o complexo I κ B/NF- κ B, permitindo o transporte do fator de transcrição NF- κ B para o núcleo e, consequentemente, ativando genes atroficos e favorecendo a degradação proteica (LIPINA; HUNDAL, 2017).

Além disso, maior concentração de AGS nos miócitos estão associados com resistência à insulina mesmo em pacientes sem diabetes (MANCO; MINGRONE; GRECO; CAPRISTO *et al.*, 2000), cuja desordem pode prejudicar os mecanismos de hipertrofia muscular (SHOU; CHEN; XIAO, 2020). Este estímulo pró-inflamatório e a supressão da sinalização da insulina nos miócitos induzidos pelos AGS reduz a atividade dos principais transportadores de nutrientes

responsáveis pela captação de aminoácidos (por exemplo, o transportador de aminoácidos neutros acoplado ao sódio) e aumenta a expressão de atrogina-1/MAFbx e MURF1 (isto é, genes pró-atróficos), paralelamente, atenuando a síntese proteica muscular ao inibir a sinalização dependente do complexo mTOR/p70-S6 quinase 1, cujos processos podem justificar a redução clínica de massa muscular (LIPINA; HUNDAL, 2017).

2.4. Índice de massa magra apendicular

Mensurar a massa muscular é um desafio no cenário clínico, pois o padrão-ouro consiste em técnicas de alto custo, como a ressonância magnética e a tomografia computadorizada (KURIYAN, 2018). Irrefutavelmente, a dissecação cadavérica, por sua vez, é impraticável na configuração de prognósticos, dado que é uma área de estudo post-mortem (CLARYS; MARTIN; MARFELL-JONES; JANSSENS *et al.*, 1999).

Assim sendo, o IMMA surgiu como um meio útil de avaliar o status de massa muscular nos cenários clínicos e epidemiológicos (CHEN; SHIVAPPA; DONG; MING *et al.*, 2021; KIM; JANG; LIM, 2016; SERGI; DE RUI; VERONESE; BOLZETTA *et al.*, 2015). Calcula-se o IMMA através da divisão da massa magra de pernas e braços pela estatura ao quadrado; por isso, esta é uma forma confiável para avaliar a hipertrofia muscular esquelética por excluir regiões viscerais e focar em regiões periféricas, desempenhando assim um papel importante em intervenções clínicas, bem como em estudos prognósticos e transversais (BUSCEMI; FERRO; PUJIA; MAZZA *et al.*, 2021; DE BRANCO; ROSSATO; RINALDI; AZEREDO *et al.*, 2022; MITCHELL; MILAN; MITCHELL; ZENG *et al.*, 2017).

Apesar da análise corporal por absorptometria de raios-x de dupla energia (DXA) não conseguir distinguir o músculo de outros tipos de massa livre de gordura, assim quantificando a retenção de líquidos, fibrose e gordura intramuscular como massa magra (SZULC; MUNOZ; MARCHAND; CHAPURLAT *et al.*, 2010), esta é uma técnica viável e de considerável aceitabilidade científica para analisar a massa magra e usá-la no cálculo do IMMA (SERGI; TREVISAN; VERONESE; LUCATO *et al.*, 2016).

2.5. Força de preensão manual

A força muscular é imperativa no ser humano como uma ferramenta clínica associada com melhor capacidade funcional por aprimorar a realização de atividades físicas e melhor bem-estar (IZQUIERDO; MERCHANT; MORLEY; ANKER *et al.*, 2021; PAPIOL; SERRA-PRAT; VICO; JEREZ *et al.*, 2016). De forma alarmante, a baixa força muscular está associada com desfechos críticos, tais como hospitalização e mortalidade relacionadas com quedas (BALOGUN; WINZENBERG; WILLS; SCOTT *et al.*, 2017). De fato, a força muscular vem se destacando como um parâmetro clínico e epidemiológico, tanto que foi considerada como o componente de sarcopenia de maior importância – superando a massa magra (CRUZ-JENTOFT; BAHAT; BAUER; BOIRIE *et al.*, 2019).

A FPM, mensurada por dinamômetro hidráulico, é um dos principais meios de examinar a força muscular, cujo teste é rápido, barato, e o equipamento é portátil (TATANGELO; MUOLLO; GHIOTTO; SCHENA *et al.*, 2022). Posto que a redução de força é originada principalmente do declínio da função muscular das extremidades do corpo devido a alterações neuromusculares (REID;

PASHA; DOROS; CLARK *et al.*, 2014), de fato, a FPM merece consideração nos âmbitos práticos e científicos (STRANDKVIST; LARSSON; PAUELSEN; NYBERG *et al.*, 2021). Ademais, é um dos principais meios de mensurar a força associada com melhoras cardiovasculares e de redução de mortalidade (LEONG; TEO; RANGARAJAN; LOPEZ-JARAMILLO *et al.*, 2015).

2.6. *Consumo de ácidos graxos saturados e índice de massa magra apendicular*

Vários estudos observacionais mostraram associações negativas entre consumo de AGS com o IMMA e parâmetros musculares relacionados (ARIAS-FERNÁNDEZ; STRUIJK; RODRÍGUEZ-ARTALEJO; LOPEZ-GARCIA *et al.*, 2020; MONTIEL-ROJAS; SANTORO; NILSSON; FRANCESCHI *et al.*, 2020; SCOTT; BLIZZARD; FELL; GILES *et al.*, 2010; WELCH; MACGREGOR; MINIHANE; SKINNER *et al.*, 2014). Em uma coorte prospectiva australiana de pacientes de meia idade e idosos (n = 1099), a ingestão de AGS foi negativamente associada com o IMMA (SCOTT; BLIZZARD; FELL; GILES *et al.*, 2010). Em um estudo transversal britânico de mulheres adultas e idosas (n = 2689), o IMMA e a massa livre de gordura foram mais baixos nos quintis mais elevados do consumo de AGS (WELCH; MACGREGOR; MINIHANE; SKINNER *et al.*, 2014). Em uma coorte de idosos europeus (n = 986), a substituição das AGS dietéticos por ácidos graxos poliinsaturados melhorou a pontuação de risco de sarcopenia (massa muscular esquelética e FPM) (MONTIEL-ROJAS; SANTORO; NILSSON; FRANCESCHI *et al.*, 2020).

2.7. *Consumo de ácidos graxos saturados e força de preensão manual*

Em aproximadamente 68.000 indivíduos com ≥ 60 anos de uma análise transversal do *UK Biobank*, os AGS dietéticos não foram associados com a FPM nem em mulheres ou em homens (GEDMANTAITE; CELIS-MORALES; HO; PELL *et al.*, 2020). Em uma coorte prospectiva espanhola com cerca de 1900 indivíduos com idade ≥ 60 anos, em que 331 participantes desenvolveram fraqueza muscular durante um período de acompanhamento de aproximadamente cinco anos, a ingestão de AGS não foi associada com fraqueza muscular medida pela FPM, mas foi negativamente associada com a funcionalidade dos membros inferiores medida com o *Short Physical Performance Battery* (ou seja, um conjunto de equilíbrio em pé, velocidade de marcha e capacidade de levantar-se de uma cadeira) (ARIAS-FERNÁNDEZ; STRUIJK; RODRÍGUEZ-ARTALEJO; LOPEZ-GARCIA *et al.*, 2020).

2.8. *Concentrações plasmáticas de ácidos graxos saturados e parâmetros musculares*

A maioria dos estudos que analisou a associação dos AGS com massa ou força muscular não dosaram os AGS circulantes, focando apenas no consumo dietético (ARIAS-FERNÁNDEZ; STRUIJK; RODRÍGUEZ-ARTALEJO; LOPEZ-GARCIA *et al.*, 2020; GEDMANTAITE; CELIS-MORALES; HO; PELL *et al.*, 2020; MONTIEL-ROJAS; SANTORO; NILSSON; FRANCESCHI *et al.*, 2020; SCOTT; BLIZZARD; FELL; GILES *et al.*, 2010; WELCH; MACGREGOR; MINIHANE; SKINNER *et al.*, 2014). Aparentemente, apenas um estudo dosou os AGS circulantes neste âmbito (ABBATECOLA; CHERUBINI; GURALNIK; ANDRES LACUEVA *et al.*, 2009). Este foi um estudo epidemiológico de italianos idosos no qual menores níveis plasmáticos de AGS foram associados com maior

capacidade funcional dos membros inferiores dada por uma pontuação do *Short Physical Performance Battery* maior que nove, ao passo que os níveis plasmáticos de AGS foram associados com um tempo maior no teste de caminhada de sete metros (ABBATECOLA; CHERUBINI; GURALNIK; ANDRES LACUEVA *et al.*, 2009).

Visto que a avaliação da ingestão alimentar através de questionários é suscetível a subrelatos (MACDIARMID; BLUNDELL, 1998; WATERWORTH; KERR; MCMANUS; COSTELLO *et al.*, 2022), é crucial o desenvolvimento de novos estudos para elucidar as associações das doses circulantes dos AGS com a força e massa muscular.

Vale enfatizar que os AGS podem ser classificados de acordo com os átomos de carbono: AGS de cadeia curta (1–6 carbonos) (SCHÖNFELD; WOJTCZAK, 2016), AGS de cadeia média (7–12 carbonos) (SCHÖNFELD; WOJTCZAK, 2016), AGS de cadeia longa (13–21 carbonos) (HIDALGO; CARRETTA; BURGOS, 2021) e AGS de cadeia muito longa (22 carbonos ou mais) (KIHARA, 2012), de modo que exercem um papel prognóstico diferente (FERNANDEZ; WEST, 2005; LAI; YEHA; SEMNANI-AZAD; MEJIA *et al.*, 2023; LEMAITRE; FRETTS; SITLANI; BIGGS *et al.*, 2015; LI; LEI; JIANG; FAN *et al.*, 2022). Portanto, além dos AGS plasmáticos totais, analisar associações de seus diversos com parâmetros musculares é promissor para melhor entendimento biológico.

2.9. População americana

Apesar da redução do consumo de AGS pela população norte-americana nos últimos anos, dados do NHANES mostram um consumo médio um pouco

superior (~11% do valor energético total, ~26-28 g/d) àquele endossado por diretrizes (<10% do valor energético total) (LIU; FORD; HU; ZELMAN *et al.*, 2017; SNETSELAAR; DE JESUS; DESILVA; STOODY, 2021). Por se tratar de média, é concebível a presença de um consumo de AGS alarmante em milhares de norte-americanos.

É indubitável que a população norte-americana culturalmente tem um padrão alimentar consistente em alimentos ricos em AGS, tais como: carnes processadas, manteigas, laticínios integrais, chocolates, *fast-food* (exemplos: batata fritas e sanduíches) e outros alimentos hiperpalatáveis (DANIEL; CROSS; KOEBNICK; SINHA, 2011; GREENBERG; BUIJSSE, 2013; YU; HU, 2018), enquanto perdas progressivas e generalizadas da massa muscular esquelética, bem como piora de parâmetros relacionados, continuam a ser uma preocupação para esta população (COLL; PHU; HAJJAR; KIRK *et al.*, 2021).

O NHANES é um banco de dados de saúde pública voltado ao controle e prevenção de doenças nos Estados Unidos que permite avaliar os AGS plasmáticos, IMMA e a FPM através de um desing transversal (NHANES, 2011). Portanto, estudos abarcando estas variáveis podem nortear futuras condutas do status de AGS com parâmetros musculares em uma população de grande relevância.

3. OBJETIVOS

3.1. Objetivo geral

Analisar a associação dos AGS plasmáticos com parâmetros pragmáticos de massa e força muscular em norte-americanos. Dois estudos transversais

foram realizados, os quais foram compostos por amostra norte-americana dos dados do NHANES.

3.2. Objetivos específicos

Artigo 1: analisar a associação dos AGS plasmáticos totais e seus subtipos com o IMMA em norte-americanos.

Artigo 2: analisar a associação dos AGS plasmáticos totais e seus subtipos com a FPM em norte-americanos.

4. ARTIGOS

- 4.1. Artigo 1 (Plasma saturated fatty acids are not associated with appendicular skeletal muscle mass index in adults: NHANES 2011-2012)**

[Original Article]

Plasma saturated fatty acids are not associated with appendicular skeletal muscle mass index in adults: NHANES 2011-2012

Heitor O. Santos ¹, Rafaela Nehme ¹, Larissa S. Limirio ¹, Breno Batista-da-Silva ¹, Flávia M.S. de Branco ¹, Erick P. de Oliveira ^{1,*}

¹ Laboratory of Nutrition, Exercise and Health (LaNES), School of Medicine, Federal University of Uberlandia (UFU), Uberlandia, Minas Gerais 38400-902, Brazil.

* Corresponding author. E-mail address: erickdeoliveira@ufu.br; erick_po@yahoo.com.br (E.P. de Oliveira).

SUMMARY

Background & Aims

Saturated fatty acids (SFAs) can hinder mechanisms of skeletal muscle hypertrophy; however, little is known about the association between plasma SFAs and their subtypes with muscle mass. This study sought to investigate the cross-sectional relationship between plasma SFAs and appendicular muscle mass index (AMMI) in adults.

Methods

A cross-sectional study was conducted with 937 subjects aged 20-59 years from a subsample of the National Health and Nutrition Examination Survey (NHANES) 2011-2012. Gas chromatography-mass spectrometry was used to detect plasma total SFA and its subtypes. Dual-energy x-ray absorptiometry (DXA) was used to assess lean body mass. AMMI was calculated by dividing appendicular lean mass by height squared. Linear regression analysis was performed to evaluate the association between SFAs and AMMI adjusting for potential confounders.

Results

No association (p -value > 0.05) was observed of plasma total SFA and its subtypes (capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, margaric acid, pentadecanoic acid, arachidic acid, tricosanoic acid, lignoceric acid, and docosanoic acid) with AMMI after adjustments for energy and protein intakes, smoking, family income, diabetes, hypertension, alcohol, marital status, education level, arthritis, fat mass, physical activity, age, sex, and race.

Conclusion

Plasma SFA and its subtypes are not associated with AMMI in adults.

Keywords: arachidic acid; lipids; muscle mass; saturated fatty acids.

1. Introduction

Adequate muscle mass is associated with higher quality of life [1, 2] and is considered an indicator of general health status [3, 4]. Muscle mass is also associated with decreased risks of cardiovascular and metabolic diseases, orthopedics disorders, cancer, and mortality [5-10]. The appendicular muscle mass index (AMMI) has emerged as a useful form to evaluate muscle mass in both clinical and epidemiological scenarios [11-13]. The AMMI is calculated dividing the lean mass of legs and arms by height squared [14] and is a reliable form to evaluate skeletal muscle hypertrophy, thereby playing an important role in clinical interventions as well as in prognostic and in cross-sectional studies [15-17]. Thus, it is of paramount importance to know the main factors associated with muscle mass. Several factors can affect the muscle mass, such as physical activity level [18], chronic diseases [19], increased oxidative stress and inflammation [20], and dietary factors [21].

Regarding the association between dietary intake and muscle mass, recent studies have shown that not only protein intake [22] is associated with muscle mass in adults, but also other nutrients such as fatty acids [23]. Although the majority of studies have focused to evaluate the association between omega-3 intake and muscle mass in several populations [23-27], little is known about the association between saturated fatty acids (SFAs) intake and muscle mass in adults. SFAs can affect health due to systemic pro-inflammatory pathways [28-30] and an *in vitro* study suggests that SFAs raise inflammation in skeletal muscle [31]. Moreover, increased levels of SFAs in skeletal muscle are associated with insulin resistance even in patients without diabetes [32], and insulin resistance can impair the mechanisms of muscle hypertrophy [33].

Since increased inflammation is associated with lower muscle mass and strength [34], it is plausible to assume that increased intake of SFAs would increase inflammation and thus would affect muscle mass. In this way, a negative association between dietary SFAs and muscle mass in young and older adults has been observed in several studies [35-38], but no research has assessed circulating SFAs levels, which can be considered a more reliable form to evaluate the chronic intake of SFAs [39]. Therefore, further epidemiological research is warranted to elucidate the association of circulating SFA and its subtypes with AMMI. Such a proposal can focus on Americans due to their dietary pattern that encompasses SFA-rich foods (unprocessed or processed meat, butter, whole-fat dairy, chocolate and other hyper-palatable foods) [40-42], while progressive and generalized losses of skeletal muscle mass and related parameters remain a concern for this population [43].

That said, we performed a cross-sectional study evaluating a population survey for Americans (National Health and Nutrition Examination Survey – NHANES) to evaluate the association between plasma total SFA and its subtypes with AMMI in adults. Given the widespread SFA-induced inflammation, we hypothesized that plasma total levels of SFAs and even some individual types of SFAs would be negatively associated with AMMI.

2. Methods

2.1. *Research Design*

A cross-sectional study was carried out employing data from the NHANES, 2011-2012. NHANES is an American survey developed by the National Center for Health Statistics (NCHS) that encompasses medical and nutritional data for

noninstitutionalized subjects, with a multi-stage representative sample consisting of children and adults. Since NHANES cross-sectional data are public, further information can be assessed on the Centers for Disease Control and Prevention (CDC) website.

2.2. Subjects

From 9756 subjects enrolled for NHANES 2011-2012, a subsample of 5643 subjects for plasma fatty acids was obtained. Then, the following exclusion criteria were used for this study: 1- subjects aged under 20 years, and 2- missing information for plasma SFAs, anthropometric and body composition data. Breastfeeding mothers were also excluded. Subjects aged 60 years or older were not eligible for the NHANES survey (2011-2012) for DXA assessment, thereby older adults were not included in the present data. Thus, 937 subjects (496 men and 441 women) aged 20-59 years were included in the present study (**Figure 1**). NHANES is a public data set and all subjects provided written informed consent, consisting of approval from the National Center for Health Statistics Research Ethics Review Board (NCHS ERB) (Protocol #2011-17 for NHANES cycle 2011-2012).

2.3. Body composition

A whole-body dual-energy x-ray absorptiometry (DXA) scanning, Hologic Discovery model A densitometers (Hologic, Inc., Bedford, Massachusetts; software version Apex 3.2.), was used to assess body composition. Patients exposed to radiographic contrast material in the 7 days before the test, those with body mass over ~200 kg (450 pounds) and height over 1.96 m (6'5"), and

pregnant women were excluded from the DXA scanning. AMMI (kg/m^2) was calculated by dividing appendicular lean body mass (lean body mass of legs and arms excluding bone mass, values in kg) by height squared [14].

2.4. Plasma saturated fatty acids

Blood samples were collected after an overnight fast. An 0.5-mL sample of plasma or serum was required to allow for repeated analyses and a volume of 100 μL was required per analysis. The appropriate content of plasma or serum was dispensed into a Nalge 2.0-mL cryovial or another plastic screw-capped vial labeled with the specimen identification and stored at -70°C .

Plasma total levels of SFAs and eleven types of SFAs were evaluated by using gas chromatography–spectrometry and expressed in $\mu\text{mol/L}$. The subtypes of SFAs were capric acid (C10), lauric acid (C12), myristic acid (C14), palmitic acid (C16), stearic acid (C18), margaric acid (C17), pentadecanoic acid (C15), arachidic acid (C20), tricosanoic acid (C23), lignoceric acid (C24) and docosanoic acid (C22). Further details on plasma SFAs evaluation can be seen in the NHANES manual [44].

2.5. Dietary intake

Two 24-hour food recalls were used to assess the dietary intake of each subject. The first 24-hour food recall interview was collected in-person and the second one was recorded by telephone three to ten days later. For subjects who had two 24-hour food recalls, the mean of nutrients was calculated. For subjects who had only the first 24-hour food recall, nutrient data for this single day was calculated as well ($n=97$). Dietary data were collected using The Automated

Multiple Pass Method [45]. Such a method consists of an interview in 5 steps (quick list, forgotten foods, time and occasion, detail cycle, and final probe). USDA's Food and Nutrient Database for Dietary Studies (FNDDS) 2011-2012 was used to obtain the elements of dietary intake, such that underlying nutrient values were based on data from the USDA National Nutrient Database for Standard Reference, release 26, produced by USDA's Nutrient Data Lab (<http://www.ars.usda.gov/nutrientdata>). We evaluated the intake of total energy (kcal/d), carbohydrate (g/d), protein (g/d and g/kg/d), total fat (g/d), as well as SFAs (g/day), monounsaturated fatty acids (g/d), polyunsaturated fatty acids (g/d), omega-3 polyunsaturated fatty acids (g/d), alpha-linolenic acid (g/d), eicosapentaenoic acid (g/d), docosahexaenoic acid (g/d), linolenic acid (g/d), fiber (g/d), and alcohol (g/d).

2.6. Statistical analysis

Sociodemographic data, anthropometry, body composition, physical activity, dietary intake, medical history, and lifestyle characteristics were described for the total sample and according to tertiles of plasma total SFAs. As plasma fatty acids consist of an NHANES subsample, all statistical analyses were carried out using the "svy" command to add information about the "2-year fatty acid subsample" sample weight, primary sampling units, and strata for correct variance estimation. A missing category was used for smoking status, annual family income, arthritis, hypertension, and diabetes in order to categorize subjects who had missing data on these variables. Comparison across tertiles of plasma total levels of SFAs was performed using linear regression analysis. Continuous variables were described

as mean and standard deviation, while categorical variables were described as percentage and confidence interval.

Linear regression analysis (coefficients and 95% confidence intervals) was performed to evaluate the association of plasma total SFAs and their individual types with AMMI. Crude (model 1) and fully adjusted (model 2) analyses were carried out. Fully statistical adjustment covered the following confounding factors: age (years), race (non-Hispanic white, non-Hispanic black, Mexican American, other Hispanic, among other races), marital status (married or living with a partner versus widowed, divorced, separated, or never married), educational level (high school graduate or under versus some college or above), and annual family income (0 to \$19,999, \$20,000 to 54,999, 55,000 to 74,999 or over \$75,000); diabetes (pre-diabetes, yes or no), arthritis (yes or no), hypertension (presence or absence), smoking status (yes or no) and physical activity level rated as moderate and vigorous exercises (yes or no); total energy (kcal/d), total protein (g/d), and alcohol (g/day); body fat mass (kg). P-values <0.05 indicated significant associations. Stata software version 14.0 (StataCorp, College Station, TX, USA) was used for obtaining all statistical analyses.

3. Results

Subject characteristics are described in **Table 1**, where data are divided into tertiles of plasma total levels of SFAs. The individuals in upper tertiles of plasma total SFAs had higher age, as well as a high prevalence of non-Hispanic whites, married/living with partner, non-menopausal women (regarding women status), arthritis and smoking, when compared to the lower tertile. Concerning anthropometric characteristics and body composition, higher values of body

mass, BMI, WC, total fat, and AMMI were observed in the upper tertiles of plasma total SFAs. Higher levels of all individual types of plasma SFAs (capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, margaric acid, pentadecanoic acid, arachidic acid, tricosanoic acid, lignoceric acid, and docosanoic acid) were observed in higher tertiles of plasma total SFAs. Regarding dietary intake, a lower intake of PUFAs, omega-3 fatty acids, alpha-linolenic acid, and linoleic acid, along with a higher intake of alcohol was observed in the upper tertiles of total plasma SFAs. In addition, individuals in higher tertiles presented a higher protein intake (g/kg) (**Table 1**).

Linear regression analyses evaluating continuous values are displayed in **Table 2**. Plasma levels of total SFAs, palmitic acid, stearic acid, and margaric acid were positively associated, while tricosanoic acid was inversely associated with AMMI in model 1 (crude analysis). However, SFA and its subtypes were not associated with AMMI after adjustments for confounders (model 2).

Additionally, the linear regression according to tertiles of SFA and its subtypes can be seen in **Table 3**. Higher tertiles of plasma total SFA, palmitic acid, and tricosanoic acid levels were associated with AMMI in the crude model (model 1); however, these associations were no longer significant after adjustments for confounders (model 2). In addition, a low ($p = 0.052$) and inverse association was observed between tertiles of arachidic acid levels and AMMI after adjustments for confounders (model 2).

4. Discussion

This study aimed to verify the association between plasma levels of total SFA and its subtypes with AMMI in adults. We hypothesized that plasma total

levels of SFA as well as its individual types would be negatively associated with the AMMI, as SFA induces inflammation at the cellular (myocyte) level, suppresses insulin signaling, downregulates activity of key nutrient transporters responsible for amino acid uptake (e.g., sodium-coupled neutral amino acid transporter, increases expression of pro-atrophic genes (e.g., atrogin-1/MAFbx and MURF1), declines protein synthesis by inhibiting mTOR/p70-S6 kinase 1-dependent signaling, and may reduce cell size and muscle mass [46]. However, although several mechanisms of SFA-induced skeletal muscle loss are suggested, we did not observe significant associations either for plasma total SFAs or their individual types with AMMI. This lack of association can be possible explained because the muscle mass loss induced by increased inflammation, insulin resistance and/or anabolic resistance occurs mainly in older adults or in specific clinical populations [47, 48], and may have few effects on muscle mass loss of general adults. Future studies should be performed evaluating the association between plasma SFAs and muscle mass in other populations, such as older adults and individuals with muscle-wasting diseases.

Concerning the diseases in our sample, a small-to-modest prevalence of diabetes, hypertension, and arthritis was observed (~5%, ~22%, ~14%, respectively), whose ailments can affect muscle mass and its related parameters due to abnormalities in insulin resistance, oxidative stress, and skeletal muscle circulation [49-51]. Nevertheless, we adjusted the results for these diseases. In addition, excess body fat accumulation may affect muscle mass by virtue of a broad crosstalk relationship between adipokines and myokines [52]. On average, the individuals of the present study had overweight or class 1 obesity according to BMI (~28 kg/m²) and total body fat mass (~31%), respectively, along with

abdominal obesity according to the waist circumference (~96 cm). Therefore, the results were also adjusted for fat mass in order to provide better reliability and specificity.

Contrary to the results of the present study, other observational studies have shown negative associations between dietary SFAs and muscle parameters [35-38]. In an Australian prospective cohort study evaluating 1099 noninstitutionalized men and women aged 50–79 years, a negative association was observed between SFA intake and AMMI [38]. In a British cross-sectional cohort study comprising 2689 women aged 18–79 years, fat-free mass index and fat-free mass were lower in the highest quintiles of dietary saturated fatty acids after adjustments for confounders [37]. A favorable impact of replacing dietary SFAs with polyunsaturated fatty acids on sarcopenia risk score (skeletal muscle mass and handgrip strength) was found in a cohort study consisting of 986 European, non-frail, older men and women [35]. Although is not fully clear, some differences between the present and other studies [35, 37, 38] can explain the discrepant results. The present study had a cross-sectional design, evaluated adults from the USA aged up to 59 y, and SFAs intake was evaluated through plasma levels; while the other studies [35, 37, 38] had a longitudinal design, evaluated both older and young adults, and dietary SFAs was evaluated through questionnaires. Thus, future longitudinal studies evaluating the association of plasma SFAs and muscle mass are needed to confirm our results.

Despite neutral associations between plasma total SFAs and their individual types with AMMI in linear regression evaluating the continuous values of the variables, when we divided the SFAs and their types into tertiles a weak and inverse association was observed between plasma arachidic acid levels and

AMMI; although the p-value ($p = 0.052$) was borderline for statistical significance. Arachidic acid (also named eicosanoic acid or icosanoic acid) is an SFA consisting of a 20-carbon chain (C 20:0) and accounts only for ~0.5% of the plasma total phospholipid fatty acids [53], while its physiological and clinical functions are incipient mainly in the field of skeletal muscle mass and related parameters. To the best of our knowledge, no study has evaluated the association of arachidic acid levels with muscle mass, but erythrocyte arachidic acid levels has been associated with an elevated risk of type 2 diabetes [54], which indicates a possible effect on insulin resistance, that would have possible effects on muscle mass, although this is only speculative. Since the association between tertiles of arachidic acid and muscle mass was weak ($p = 0.052$) and no association was observed evaluating the continuous values, we did not consider that arachidic acid can have relevant clinical effects on muscle mass.

The present study has limitations. The cross-sectional design does not allow to infer causality. We did not measure directly the muscle mass. DXA scanning was used to evaluate the lean body mass used in AMMI. Although DXA scanning cannot evaluate muscle mass, such a method is viable for assessing lean body mass, with the advantages of a straightforward technology, quick assessment, and a low radiation dose compared to gold-standard techniques [55]. Low grade-inflammation was not assessed, which could help to explain our results. The results cannot be extrapolated to older adults as we did not evaluate subjects aged ≥ 60 years due to the absence of DXA evaluation in NHANES database. Last but not least, our results cannot be translated into different populations, since the NHANES survey covers a representative sample in the USA; however, the USA is a continental country with efforts toward scientific

progress whereby our data may be useful for expanding particular clinical and epidemiological aspects. As for strengths, this study is a novelty, as associations between circulating SFAs and their individual types with muscle mass remain an area to be elucidated. Furthermore, the sample size ($n = 937$) is viable taking into account the principles of observational research.

5. Conclusion

Plasma total levels of SFAs and their individual types are not associated with AMMI in young and middle-aged adults. Further research is warranted to investigate the relationship between plasma total levels of SFAs and their individual types in other populations such as older adults and subjects at high risk of pathophysiological muscle wasting.

Funding

None.

Author contributions

HOS wrote the manuscript; RN, LSL, BBS, FMSB performed statistical and participated in data description; EPO wrote, participated in the interpretation of the data and revision of the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors declare no conflicts of interest.

Acknowledgements

We thank CAPES for the financial support. EPO would like to thank The Brazilian National Council for Scientific and Technological Development (CNPq, Brazil, 304205/2019-2).

References

1. Trombetti A, Reid KF, Hars M, Herrmann FR, Pasha E, Phillips EM, Fielding RA: **Age-associated declines in muscle mass, strength, power, and physical performance: impact on fear of falling and quality of life.** *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2016, **27**(2):463-471.
2. Thiebaud RS, Loenneke JP, Abe T, Fahs CA, Rossow LM, Kim D, Beck TW, Bemben DA, Larson RD, Bemben MG: **Appendicular lean mass and site-specific muscle loss in the extremities correlate with dynamic strength.** *Clinical physiology and functional imaging* 2017, **37**(3):328-331.
3. Wang H, Hai S, Liu Y, Liu Y, Dong B: **Skeletal Muscle Mass as a Mortality Predictor among Nonagenarians and Centenarians: A Prospective Cohort Study.** *Scientific reports* 2019, **9**(1):2420.
4. Weng CH, Tien CP, Li CI, L'Heureux A, Liu CS, Lin CH, Lin CC, Lai SW, Lai MM, Lin WY: **Mid-upper arm circumference, calf circumference and mortality in Chinese long-term care facility residents: a prospective cohort study.** *BMJ open* 2018, **8**(5):e020485.
5. Srikanthan P, Horwich TB, Calton Press M, Gornbein J, Watson KE: **Sex Differences in the Association of Body Composition and Cardiovascular Mortality.** *Journal of the American Heart Association* 2021, **10**(5):e017511.
6. Abramowitz MK, Hall CB, Amodu A, Sharma D, Androga L, Hawkins M: **Muscle mass, BMI, and mortality among adults in the United States: A population-based cohort study.** *PloS one* 2018, **13**(4):e0194697.
7. Hong S, Chang Y, Jung HS, Yun KE, Shin H, Ryu S: **Relative muscle mass and the risk of incident type 2 diabetes: A cohort study.** *PloS one* 2017, **12**(11):e0188650.
8. Psutka SP, Boorjian SA, Moynagh MR, Schmit GD, Costello BA, Thompson RH, Stewart-Merrill SB, Lohse CM, Cheville JC, Leibovich BC *et al*: **Decreased Skeletal Muscle Mass is Associated with an Increased Risk of Mortality after Radical Nephrectomy for Localized Renal Cell Cancer.** *The Journal of urology* 2016, **195**(2):270-276.
9. Kim WJ, Shin HM, Lee JS, Song DG, Lee JW, Chang SH, Park KY, Choy WS: **Sarcopenia and Back Muscle Degeneration as Risk Factors for Degenerative Adult Spinal Deformity with Sagittal Imbalance and Degenerative Spinal Disease: A Comparative Study.** *World neurosurgery* 2021, **148**:e547-e555.
10. Bokshan SL, DePasse JM, Daniels AH: **Sarcopenia in Orthopedic Surgery.** *Orthopedics* 2016, **39**(2):e295-300.
11. Sergi G, De Rui M, Veronese N, Bolzetta F, Berton L, Carraro S, Bano G, Coin A, Manzato E, Perissinotto E: **Assessing appendicular skeletal muscle mass with bioelectrical impedance analysis in free-living Caucasian older adults.** *Clinical nutrition (Edinburgh, Scotland)* 2015, **34**(4):667-673.
12. Chen L, Shivappa N, Dong X, Ming J, Zhao Q, Xu H, Liang P, Cheng M, Liu J, Sun P *et al*: **Association between appendicular skeletal muscle index and leukocyte telomere**

- length in adults: A study from National Health and Nutrition Examination Survey (NHANES) 1999-2002. *Clinical nutrition (Edinburgh, Scotland)* 2021, **40**(5):3470-3478.
13. Kim KM, Jang HC, Lim S: **Differences among skeletal muscle mass indices derived from height-, weight-, and body mass index-adjusted models in assessing sarcopenia.** *The Korean journal of internal medicine* 2016, **31**(4):643-650.
 14. Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ, Lindeman RD: **Epidemiology of sarcopenia among the elderly in New Mexico.** *American journal of epidemiology* 1998, **147**(8):755-763.
 15. Buscemi C, Ferro Y, Pujia R, Mazza E, Boragina G, Sciacqua A, Piro S, Pujia A, Sesti G, Buscemi S et al: **Sarcopenia and Appendicular Muscle Mass as Predictors of Impaired Fasting Glucose/Type 2 Diabetes in Elderly Women.** *Nutrients* 2021, **13**(6).
 16. Mitchell CJ, Milan AM, Mitchell SM, Zeng N, Ramzan F, Sharma P, Knowles SO, Roy NC, Sjödin A, Wagner KH et al: **The effects of dietary protein intake on appendicular lean mass and muscle function in elderly men: a 10-wk randomized controlled trial.** *The American journal of clinical nutrition* 2017, **106**(6):1375-1383.
 17. de Branco FMS, Rossato LT, Rinaldi AEM, Azeredo CM, de Oliveira EP: **Plasma omega-3 is not associated with appendicular muscle mass index in young and middle-aged individuals: Results from NHANES 2011-2012.** *Prostaglandins, leukotrienes, and essential fatty acids* 2022, **178**:102412.
 18. Taani MH, Strath SJ, Cho CC, Ellis J, Oh H: **Objective Physical Activity Levels, Sedentary Time, and Muscle Mass, Strength, and Function: Impact on Physical and Mental Health-Related Quality of Life in Older Adults.** *Research in gerontological nursing* 2022, **15**(3):131-139.
 19. Ebner N, Sliziuk V, Scherbakov N, Sandek A: **Muscle wasting in ageing and chronic illness.** *ESC heart failure* 2015, **2**(2):58-68.
 20. Meng SJ, Yu LJ: **Oxidative stress, molecular inflammation and sarcopenia.** *International journal of molecular sciences* 2010, **11**(4):1509-1526.
 21. Cruz-Jentoft AJ, Dawson Hughes B, Scott D, Sanders KM, Rizzoli R: **Nutritional strategies for maintaining muscle mass and strength from middle age to later life: A narrative review.** *Maturitas* 2020, **132**:57-64.
 22. Nunes EA, Colenso-Semple L, McKellar SR, Yau T, Ali MU, Fitzpatrick-Lewis D, Sherifali D, Gaudichon C, Tomé D, Atherton PJ: **Systematic review and meta-analysis of protein intake to support muscle mass and function in healthy adults.** *Journal of cachexia, sarcopenia and muscle* 2022, **13**(2):795-810.
 23. Rossato LT, Schoenfeld BJ, de Oliveira EP: **Is there sufficient evidence to supplement omega-3 fatty acids to increase muscle mass and strength in young and older adults?** *Clinical Nutrition* 2020, **39**(1):23-32.
 24. de Branco FM, Rossato LT, Rinaldi AEM, Azeredo CM, de Oliveira EP: **Plasma omega-3 is not associated with appendicular muscle mass index in young and middle-aged individuals: Results from NHANES 2011-2012.** *Prostaglandins, Leukotrienes and Essential Fatty Acids* 2022, **178**:102412.
 25. de Branco FM, Rinaldi AEM, Pereira JL, Roschel H, Azeredo CM, de Oliveira EP: **Plasma omega-3 fatty acids are positively associated with appendicular muscle mass index only in adults with low protein intake: Results from NHANES 2011-2012.** *Clinical Nutrition* 2023, **42**(2):76-82.
 26. Dos Reis AS, Limirio LS, Santos HO, de Oliveira EP: **Intake of polyunsaturated fatty acids and ω -3 are protective factors for sarcopenia in kidney transplant patients.** *Nutrition* 2021, **81**:110929.
 27. Rossato LT, de Branco FM, Azeredo CM, Rinaldi AEM, de Oliveira EP: **Association between omega-3 fatty acids intake and muscle strength in older adults: A study from National Health and Nutrition Examination Survey (NHANES) 1999-2002.** *Clinical Nutrition* 2020, **39**(11):3434-3441.

28. Huang S, Rutkowski JM, Snodgrass RG, Ono-Moore KD, Schneider DA, Newman JW, Adams SH, Hwang DH: **Saturated fatty acids activate TLR-mediated proinflammatory signaling pathways.** *Journal of lipid research* 2012, **53**(9):2002-2013.
29. Fritsche KL: **The science of fatty acids and inflammation.** *Advances in nutrition (Bethesda, Md)* 2015, **6**(3):293s-301s.
30. Håversen L, Danielsson KN, Fogelstrand L, Wiklund O: **Induction of proinflammatory cytokines by long-chain saturated fatty acids in human macrophages.** *Atherosclerosis* 2009, **202**(2):382-393.
31. Pillon NJ, Arane K, Bilan PJ, Chiu TT, Klip A: **Muscle cells challenged with saturated fatty acids mount an autonomous inflammatory response that activates macrophages.** *Cell communication and signaling : CCS* 2012, **10**(1):30.
32. Manco M, Mingrone G, Greco AV, Capristo E, Gniuli D, De Gaetano A, Gasbarrini G: **Insulin resistance directly correlates with increased saturated fatty acids in skeletal muscle triglycerides.** *Metabolism: clinical and experimental* 2000, **49**(2):220-224.
33. Shou J, Chen PJ, Xiao WH: **Mechanism of increased risk of insulin resistance in aging skeletal muscle.** *Diabetology & metabolic syndrome* 2020, **12**:14.
34. Tuttle CS, Thang LA, Maier AB: **Markers of inflammation and their association with muscle strength and mass: A systematic review and meta-analysis.** *Ageing research reviews* 2020, **64**:101185.
35. Montiel-Rojas D, Santoro A, Nilsson A, Franceschi C, Capri M, Bazzocchi A, Battista G, de Groot L, Feskens EJM, Berendsen AAM *et al*: **Beneficial Role of Replacing Dietary Saturated Fatty Acids with Polyunsaturated Fatty Acids in the Prevention of Sarcopenia: Findings from the NU-AGE Cohort.** *Nutrients* 2020, **12**(10).
36. Arias-Fernández L, Struijk EA, Rodríguez-Artalejo F, Lopez-Garcia E, Lana A: **Habitual dietary fat intake and risk of muscle weakness and lower-extremity functional impairment in older adults: A prospective cohort study.** *Clinical nutrition (Edinburgh, Scotland)* 2020, **39**(12):3663-3670.
37. Welch AA, MacGregor AJ, Minihane AM, Skinner J, Valdes AA, Spector TD, Cassidy A: **Dietary fat and fatty acid profile are associated with indices of skeletal muscle mass in women aged 18-79 years.** *The Journal of nutrition* 2014, **144**(3):327-334.
38. Scott D, Blizzard L, Fell J, Giles G, Jones G: **Associations between dietary nutrient intake and muscle mass and strength in community-dwelling older adults: the Tasmanian Older Adult Cohort Study.** *Journal of the American Geriatrics Society* 2010, **58**(11):2129-2134.
39. Arab L: **Biomarkers of fat and fatty acid intake.** *The Journal of nutrition* 2003, **133** Suppl 3(3):925s-932s.
40. Yu E, Hu FB: **Dairy Products, Dairy Fatty Acids, and the Prevention of Cardiometabolic Disease: a Review of Recent Evidence.** *Current atherosclerosis reports* 2018, **20**(5):24.
41. Daniel CR, Cross AJ, Koebnick C, Sinha R: **Trends in meat consumption in the USA.** *Public health nutrition* 2011, **14**(4):575-583.
42. Greenberg JA, Buijsse B: **Habitual chocolate consumption may increase body weight in a dose-response manner.** *PloS one* 2013, **8**(8):e70271.
43. Coll PP, Phu S, Hajjar SH, Kirk B, Duque G, Taxel P: **The prevention of osteoporosis and sarcopenia in older adults.** *Journal of the American Geriatrics Society* 2021, **69**(5):1388-1398.
44. NHANES: **Laboratory Procedure Manual.** 2011.
45. Moshfegh AJ, Rhodes DG, Baer DJ, Murayi T, Clemens JC, Rumpler WV, Paul DR, Sebastian RS, Kuczynski KJ, Ingwersen LA *et al*: **The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes.** *The American journal of clinical nutrition* 2008, **88**(2):324-332.
46. Lipina C, Hundal HS: **Lipid modulation of skeletal muscle mass and function.** *Journal of cachexia, sarcopenia and muscle* 2017, **8**(2):190-201.

47. Peake J, Della Gatta P, Cameron-Smith D: **Aging and its effects on inflammation in skeletal muscle at rest and following exercise-induced muscle injury.** *American journal of physiology Regulatory, integrative and comparative physiology* 2010, **298**(6):R1485-1495.
48. Londhe P, Guttridge DC: **Inflammation induced loss of skeletal muscle.** *Bone* 2015, **80**:131-142.
49. Nishitani M, Shimada K, Sunayama S, Masaki Y, Kume A, Fukao K, Sai E, Yamashita H, Ohmura H, Onishi T *et al*: **Impact of diabetes on muscle mass, muscle strength, and exercise tolerance in patients after coronary artery bypass grafting.** *Journal of cardiology* 2011, **58**(2):173-180.
50. Kara M, Kara Ö, Ceran Y, Kaymak B, Kaya TC, Çıtır BN, Durmuş ME, Durmuşoğlu E, Razaq S, Doğan Y *et al*: **SARcopenia Assessment in Hypertension: The SARAH Study.** *American journal of physical medicine & rehabilitation* 2023, **102**(2):130-136.
51. Andonian BJ, Huffman KM: **Skeletal muscle disease in rheumatoid arthritis: the center of cardiometabolic comorbidities?** *Current opinion in rheumatology* 2020, **32**(3):297-306.
52. Chung HS, Choi KM: **Adipokines and Myokines: A Pivotal Role in Metabolic and Cardiovascular Disorders.** *Current medicinal chemistry* 2018, **25**(20):2401-2415.
53. Information NCfB: **PubChem Compound Summary for CID 10467, Arachidic acid. Retrieved February 22, 2023 from <https://pubchem.ncbi.nlm.nih.gov/compound/Arachidic-acid>.** 2023.
54. Lin JS, Dong HL, Chen GD, Chen ZY, Dong XW, Zheng JS, Chen YM: **Erythrocyte Saturated Fatty Acids and Incident Type 2 Diabetes in Chinese Men and Women: A Prospective Cohort Study.** *Nutrients* 2018, **10**(10).
55. Sergi G, Trevisan C, Veronese N, Lucato P, Manzato E: **Imaging of sarcopenia.** *European journal of radiology* 2016, **85**(8):1519-1524.

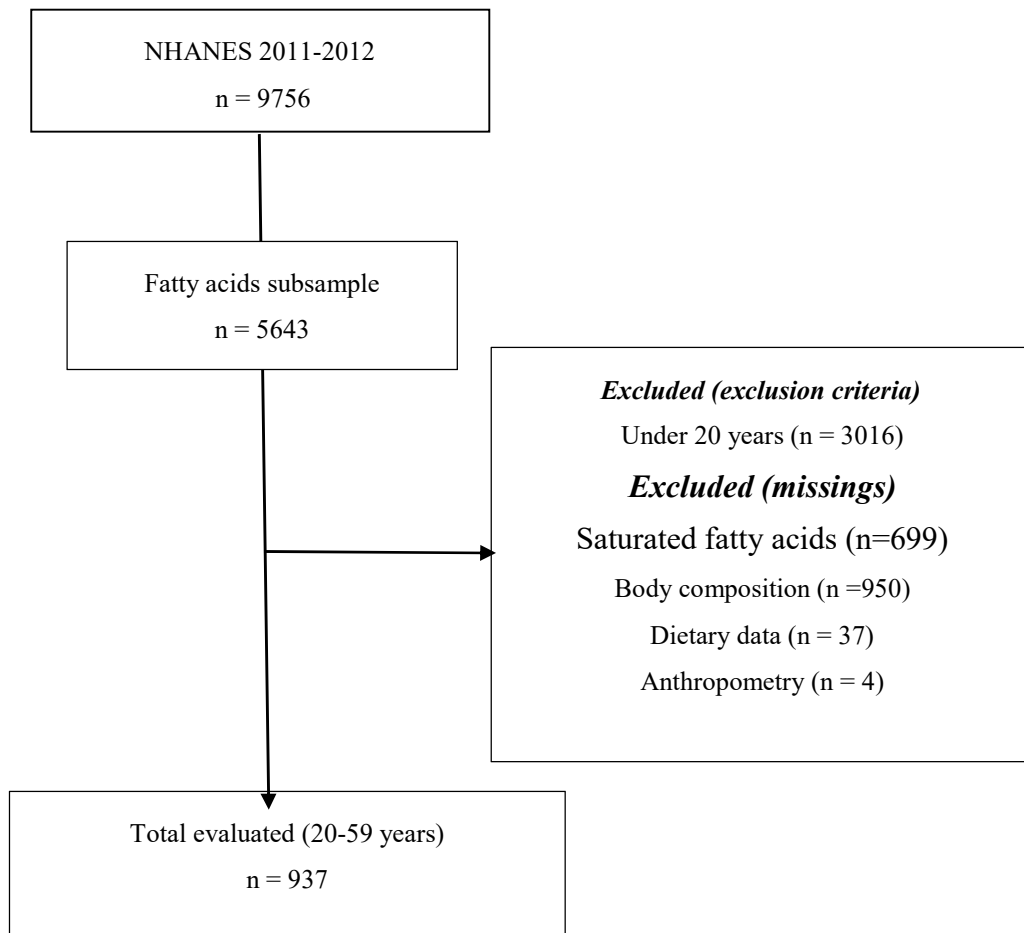


Figure 1. Flowchart of the subjects evaluated. Sample selection from NHANES, 2011-2012.

Table 1. Sociodemographic, body composition, anthropometric, and dietary characteristics the in total sample and according to plasma total saturated fatty acids levels. Data from NHANES (2011-2012).

Variables	Total	Tertile 1	Tertile 2	Tertile 3	p-Value
Plasma saturated fatty acids, $\mu\text{mol/L}$	4017.4 $\pm$ 1367.5	2831.2 $\pm$ 335.9	3723.6 $\pm$ 242.5	5395.9 $\pm$ 1418.5	<0.001
Sociodemographic Characteristics					
Age, y	39.1 $\pm$ 11.7	34.6 $\pm$ 11.7	40.1 $\pm$ 11.1	42 $\pm$ 11.2	<0.001
Sex, %					0.067
Women	51.7 (46.9; 56.4)	49.3 (43.5; 55.1)	48.1 (39.5; 56.9)	57.5 (50.1; 64.6)	0.014
Men	48.3 (43.6; 53.1)	50.7 (44.9; 56.5)	51.9 (43.1; 60.5)	42.5 (35.4; 49.9)	
Race/ethnicity, %					0.033
Non-Hispanic white	64.4 (55.8; 72.2)	56.9 (47; 66.3)	67.8 (57.2; 76.9)	67.7 (59.2; 75.1)	0.324
Marital status, %					
Married/Living with Partner	60.3 (54.6; 65.7)	51.9 (44.2; 59.5)	61.2 (51.1; 70.5)	66.9 (55.9; 76.3)	0.324
Single/Divorced/Widowed/Never Married	39.7 (34.3; 45.4)	48.1 (40.5; 55.8)	38.8 (29.5; 48.9)	33.1 (23.7; 44.1)	
Annual Family Income, %					
\$0-19,999	19.9 (14.8; 26.2)	24.8 (16.1; 36.2)	16.7 (11.9; 23)	18.8 (12.5; 27.1)	
\$20,000-54,999	32 (27; 37.4)	27.8 (20.2; 37)	34 (27.6; 40.9)	33.8 (27.5; 40.7)	
Over \$55,000	12.1 (8.8; 16.4)	8.8 (5.7; 13.3)	14 (8.4; 22.5)	13 (7.8; 21.1)	0.324
Over \$75,000	33.3 (27.1; 40.3)	35.7 (25.8; 47)	33.2 (23.6; 44.4)	31.3 (24.7; 38.9)	
Missing	2.7 (2; 3.7)	2.9 (1.2; 6.7)	2.2 (0.9; 5.3)	3.1 (1.1; 8.3)	
Health Conditions and Behavior					
Diabetes, %					0.068
No	93.5 (91.4; 95.2)	94.8 (90.5; 97.2)	96.9 (94.9; 98.2)	88.9 (83.2; 92.8)	0.076
Yes	5.4 (3.7; 7.8)	4.5 (2.2; 8.9)	2.6 (1.6; 4.1)	9.2 (5.8; 14.3)	
Pre-diabetes	1 (0.3; 3.5)	0.8 (0.3; 2.2)	0.3 (0.1; 1.4)	1.9 (0.3; 11.1)	
Missing	0.0005 (0.00006; 0.0046)	-	0.001 (0.001; 0.012)	-	
Hypertension, %					0.008
No	77.6 (71.9; 82.4)	81.6 (74.4; 87.2)	78 (71.4; 83.4)	73.5 (63.1; 81.8)	
Yes	22.4 (17.6; 28)	18.4 (12.8; 25.6)	22 (16.6; 28.6)	26.4 (18.2; 36.8)	
Missing	0.0003 (0.00003; 0.00253)	-	-	0.0009 (0.0001; 0.007)	
Menopause, %					0.017
No	67.8 (59.4; 75.1)	51.9 (44.2; 59.5)	61.2 (51.1; 70.5)	66.9 (55.9; 76.3)	
Yes	31.6 (24.9; 39.2)	48.1 (40.5; 55.8)	38.8 (29.5; 48.9)	33.1 (23.7; 44.1)	
Arthritis, %					
No	86.1 (83.2; 88.6)	89.6 (83; 93.8)	86.9 (80.1; 91.7)	82.2 (76.6; 86.7)	0.143
Yes	13.8 (11.3; 16.6)	10.1 (6; 16.7)	13.1 (8.3; 19.9)	17.8 (13.3; 23.4)	
Physical activity, %		0.002 (0.0003; 0.02)	-	-	<0.001
Yes	45.4 (41.1; 49.7)	42.3 (34.3; 50.8)	43.6 (36.9; 50.5)	49.9 (43.3; 56.6)	
No	54.6 (50.3; 58.9)	57.7 (49.2; 65.7)	56.4 (49.5; 63.1)	50.1 (43.4; 56.7)	
Smoking status, %					

No	77.5 (72.9; 81.5)	84.3 (78.1; 89.1)	79 (72.2; 84.5)	69.7 (63.7; 75.1)	
Yes	22.5 (18.4; 27.1)	15.7 (10.9; 21.9)	20.8 (15.3; 27.6)	30.3 (24.9; 36.3)	
		-	0.002 (0.0002; 0.01)	-	
Anthropometric Characteristics and Body Composition					
Body Mass, kg	81.7 ± 19.7	77.8 ± 21.6	81.8 ± 18.6	85.1 ± 18.6	0.001
Height, m	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	0.873
Body mass index, kg/m ²	28.1 ± 6	26.7 ± 6.7	28.3 ± 5.5	29.2 ± 5.6	<0.001
Waist circumference (cm)	96.2 ± 15.1	91.3 ± 16.8	96.6 ± 13.4	100.4 ± 14	<0.001
Total fat mass, kg	27.0 ± 10.7	24.8 ± 12.4	27.5 ± 9.9	28.3 ± 9.6	0.001
Total fat mass, %	32.4 ± 8.1	30.9 ± 9.4	33.2 ± 7.6	33 ± 7.3	0.007
Lean mass, kg	52.7 ± 12.8	51.0 ± 13.3	52.3 ± 12.3	54.8 ± 12.7	0.007
Appendicular muscle mass index, kg/m ²	7.9 ± 1.6	7.7 ± 1.8	7.8 ± 1.5	8.1 ± 1.5	0.028
Plasma fatty acids					
Total saturated fatty acids, µmol/L	4017.4 ± 1367.5	2831.2 ± 335.9	3723.6 ± 242.5	5395.9 ± 1418.5	<0.001
Capric acid, µmol/L	3.0 ± 5.1	1.6 ± 1.1	1.9 ± 1.0	5.5 ± 8.0	<0.001
Lauric acid, µmol/L	13.9 ± 19.4	6.8 ± 7.5	10.1 ± 9.2	24.3 ± 27.8	<0.001
Myristic acid, µmol/L	141.9 ± 102.3	73.8 ± 28.6	113.8 ± 32.6	232.9 ± 122.9	<0.001
Palmitic acid, µmol/L	2928.6 ± 1061.4	2021.1 ± 257	2699.8 ± 210.4	3987.6 ± 1117.0	<0.001
Stearic acid, µmol/L	694.4 ± 195.3	529.2 ± 73.1	661.4 ± 78.7	877.9 ± 200.2	<0.001
Margaric acid, µmol/L	31.2 ± 9.3	24.7 ± 4.4	29.6 ± 5.7	38.6 ± 10.3	<0.001
Pentadecanoic acid, µmol/L	24.9 ± 10.9	17.5 ± 5.9	23.1 ± 6.4	33.5 ± 12.1	<0.001
Arachidic acid, µmol/L	23.7 ± 5.4	20.4 ± 3.7	23.8 ± 4.6	26.5 ± 5.9	<0.001
Tricosanoic acid, µmol/L	29.0 ± 7.5	25.2 ± 5.7	29.8 ± 7.0	31.6 ± 7.9	<0.001
Lignoceric acid, µmol/L	58.5 ± 14.3	50.8 ± 10.8	60.3 ± 13.0	63.6 ± 15.0	<0.001
Docosanoic acid, µmol/L	68.3 ± 17.0	60.0 ± 13.1	70.1 ± 15.1	73.8 ± 18.7	<0.001
Dietary Intake					
Energy, kcal/d	2210.6 ± 850.3	2239.1 ± 898.7	2154.6 ± 831	2243 ± 822.7	0.923
Carbohydrate, g/d	268.9 ± 107.5	271.8 ± 117.3	268.3 ± 106.8	267 ± 99.2	0.515
Protein, g/d	85.6 ± 36.4	86.9 ± 38.8	83.2 ± 35.3	87.0 ± 35.3	0.95
Protein, g/kg	1.1 ± 0.5	1.2 ± 0.6	1.0 ± 0.5	1.1 ± 0.4	0.03
Total fat, g/d	82.9 ± 39.7	86.7 ± 42	79.8 ± 38.2	82.7 ± 38.8	0.351
Cholesterol, mg/d	280 ± 189.9	292.2 ± 194.3	268.7 ± 200.7	280.6 ± 172	0.504
Saturated fatty acids, g/d	26.7 ± 13.6	27.3 ± 14.4	25.4 ± 13	27.6 ± 13.5	0.778
Monounsaturated fats, g/d	29.6 ± 15.1	31.0 ± 16	28.7 ± 14.7	29.4 ± 14.8	0.355
Polyunsaturated fatty acids, g/d	19.6 ± 10.9	21.1 ± 11.7	19.2 ± 10.5	18.8 ± 10.4	0.038
Sugar, g/d	116.3 ± 66.2	116.5 ± 69.1	119.7 ± 67.5	112.5 ± 61.8	0.517
Omega-3 polyunsaturated fatty acids, g/d	1.89 ± 1.1	2.09 ± 1.35	1.79 ± 0.99	1.81 ± 0.96	0.01
Alpha-linolenic acid, g/d	1.8 ± 1.06	2.01 ± 1.32	1.71 ± 0.95	1.71 ± 0.91	0.004
Eicosapentaenoic acid, g/d	0.03 ± 0.07	0.02 ± 0.05	0.02 ± 0.05	0.03 ± 0.09	0.388
Docosahexaenoic acid, g/d	0.06 ± 0.13	0.06 ± 0.12	0.05 ± 0.12	0.06 ± 0.14	0.708
Linoleic acid, g/d	17.4 ± 9.8	18.6 ± 10.4	17.0 ± 9.6	16.7 ± 9.5	0.047

Total fiber (g/d)	18.4 ± 9.4	18.4 ± 10	18.3 ± 9	18.7 ± 9.4	0.748
Alcohol, g/d	10.8 ± 23.7	7.4 ± 22	8.8 ± 20.7	15.9 ± 26.8	0.002

Data are described as mean (standard deviation) or percentage (confidence interval).

Table 2. Linear regression between appendicular muscle mass index with plasma total SFAs and their individual types. Results from NHANES (2011-2012).

Model 1: crude analysis. Model 2: each variable was adjusted for energy intake, protein intake, smoking, family income,

Plasma fatty acids	Model 1		Model 2	
	β (95%CI)	<i>p</i> -value	β (95%CI)	<i>p</i> -value
Saturated	0.0001 (0.0; 0.0002)	0.014	-0.0003 (-0.00009; 0.00002)	0.258
Lauric Acid	0.001 (-0.004; 0.007)	0.523	-0.001 (-0.004;0.008)	0.173
Palmitic acid	0.0001 (0.0; 0.0003)	0.011	-0.00003 (-0.0001; 0.00004)	0.366
Capric acid	0.014 (-0.01; 0.04)	0.260	-0.007 (-0.02; 0.005)	0.254
Stearic acid	0.0006 (0.0001; 0.001)	0.015	-0.0004 (-0.0009; 0.0001)	0.120
Margaric acid	0.019 (0.006; 0.032)	0.006	-0.003 (-0.012; 0.005)	0.471
Pentadecanoic acid	0.004 (-0.010; 0.019)	0.546	-0.004 (-0.013; 0.005)	0.347
Arachidic acid	-0.02 (-0.05; 0.004)	0.095	-0.019 (-0.04; 0.001)	0.070
Tricosanoic acid	-0.02 (-0.04; -0.01)	0.002	-0.091 (-0.021; 0.003)	0.143
Lignoceric acid	-0.002 (-0.009; 0.005)	0.536	-0.006 (-0.012; 0.0002)	0.057
Docosanoic acid	-0.002 (-0.010; 0.004)	0.404	-0.004 (-0.01;0.0004)	0.069
Myristic acid	0.001 (-0.0003; 0.002)	0.120	-0.0005 (-0.001; 0.0002)	0.169

diabetes, arterial hypertension, alcohol, marital status, education level, arthritis, fat mass (kg), physical activity, age, sex, and race. Data are shown as coefficients. and 95% confidence intervals (95% CI). P-values < 0.05 were considered statistically significant.

Table 3. Linear regression between AMMI and tertiles of plasma total SFAs and their individual types. Results from NHANES (2011-2012).

		Model 1 β (95%CI)			<i>p-trend</i>	Model 2 β (95%CI)			<i>p-trend</i>
		T1	T2	T3		T1	T2	T3	
Saturated	Ref.		0.13 (- 0.13;0.41)	0.36 (0.04;0.68)	0.028	Ref.	0.04 (- 0.13;0.21)	-0.02 (- 0.23;0.18)	0.799
Lauric Acid	Ref.		0.01 (- 0.35;0.38)	-0.04 (- 0.40;0.31)	0.781	Ref.	-0.01 (- 0.22;0.19)	-0.14 (- 0.32;0.04)	0.123
Palmitic acid	Ref.		0.25 (0.06;0.43)	0.44 (0.13;0.75)	0.008	Ref.	0.07 (- 0.05;0.20)	0.06 (- 0.10;0.23)	0.430
Capric acid	Ref.		0.08 (- 0.22;0.39)	-0.01 (- 0.45; 0.42)	0.962	Ref.	-0.05 (- 0.25;0.14)	-0.12 (- 0.30;0.05)	0.159
Stearic acid	Ref.		0.26 (- 0.03; 0.56)	0.27 (- 0.004;0.55)	0.053	Ref.	-0.02 (- 0.22;0.18)	-0.17 (- 0.43;0.09)	0.182
Margaric acid	Ref.		0.06 (- 0.35;0.48)	0.25 (- 0.12;0.63)	0.169	Ref.	-0.12 (- 0.33;0.08)	-0.13 (- 0.34;0.08)	0.224
Pentadecanoic acid	Ref.		-0.31 (- 0.56;-0.06)	-0.01 (- 0.37;0.34)	0.888	Ref.	-0.28 (- 0.49;- 0.07)	-0.15 (- 0.38;0.09)	0.352
Arachidic acid	Ref.		0.04 (- 0.16;0.26)	-0.27 (- 0.62;0.06)	0.109	Ref.	-0.009 (- 0.19;0.18)	-0.25 (- 0.50;- 0.002)	0.052
Tricosanoic acid	Ref.		0.001 (- 0.29;0.29)	-0.34 (- 0.61;-0.06)	0.013	Ref.	0.10 (- 0.74;0.28)	-0.04 (- 0.25;0.17)	0.667
Lignoceric acid	Ref.		0.03 (- 0.36;0.42)	-0.01 (- 0.31;0.28)	0.907	Ref.	-0.02 (- 0.23;0.19)	-0.13 (- 0.35;0.07)	0.182
Docosanoic acid	Ref.		0.23 (- 0.06;0.52)	0.01 (- 0.25;0.28)	0.948	Ref.	0.04 (- 0.16;0.2)	-0.13 (- 0.32;0.05)	0.144
Myristic acid	Ref.		0.18 (- 0.16;0.54)	0.18 (- 0.25;0.63)	0.422	Ref.	-0.03 (- 0.20;0.13)	-0.15 (- 0.35;0.06)	0.142

T, tertile. Model 1: crude analysis. Model 2: each variable was adjusted for energy intake, protein intake, smoking, family income, diabetes, arterial hypertension, alcohol, marital status, education level, arthritis, fat mass (kg), physical activity, age, sex, and race. Data are shown as coefficients. and 95% confidence intervals (95% CI). P-values < 0.05 were considered statistically significant.

4.2. Artigo 2 (Association between plasma saturated fatty acids and muscle strength in Americans aged <60 versus ≥60 years: Results from NHANES 2011-2012)

[Original Article]

Association between plasma saturated fatty acids and muscle strength in Americans aged <60 versus ≥60 years: Results from NHANES 2011-2012

Heitor O. Santos ¹, Rafaela Nehme ¹, Larissa S. Limirio ¹, Maria Eduarda de F. Mendonça ¹, Breno Batista-da-Silva ¹, Flávia M.S. de Branco ¹, Erick P. de Oliveira ^{1,*}

¹ Laboratory of Nutrition, Exercise and Health (LaNES), School of Medicine, Federal University of Uberlandia (UFU), Uberlandia, Minas Gerais 38400-902, Brazil.

* Corresponding author. E-mail address: erickdeoliveira@ufu.br; erick_po@yahoo.com.br (E.P. de Oliveira).

SUMMARY

Background & Aims

The pro-inflammatory potential of saturated fatty acids (SFAs) can affect skeletal muscle and hence its related parameters. A handful of research has investigated the association between dietary SFAs and muscle strength, such that assessing plasma SFA levels is even more incipient in this regard. Thus, we aimed to ascertain the association between plasma SFA levels and muscle strength in adults.

Methods

A cross-sectional study was performed with 1591 individuals (20-80 years) from a subsample of the National Health and Nutrition Examination Survey (NHANES) 2011-2012. Gas chromatography-mass spectrometry was used to detect plasma total SFAs and their subtypes. Muscle strength was assessed through the sum of handgrip strength. Linear regression analysis was performed to evaluate the association between plasma SFA levels according to the entire population as well as for age (<60 and ≥60 years).

Results

Plasma total SFAs and their individual types were not associated with handgrip strength in all individuals upon the adjustment model (energy intake, protein intake, smoking, family income, diabetes, arterial hypertension, alcohol, marital status, education level, arthritis, physical activity, age, sex, race, and body mass index). However, when subjects were divided according to age, negative associations were observed for capric acid (β -value = -0.2978; 95%CI = -0.5855, -0.0100; p = 0.043) and stearic acid (β -value = -0.0058; 95%CI = -0.0100, -0.0003; p = 0.038) levels only for those aged <60 years.

Conclusion

Overall, plasma total SFAs and their types were not associated with handgrip strength in Americans, except stearic acid and capric acid for those aged <60 years, which were inversely associated.

Keywords: capric acid; handgrip strength; muscle strength; saturated fatty acids; stearic acid.

1. Introduction

Muscle strength is of pivotal importance in human beings as a harbinger of falls and functionality [1]. In light of this, low muscle strength may ultimately be associated with critical medical outcomes such as fall-related hospitalization and mortality [2]. Moreover, declines in muscle function affect welfare by hindering the capacity to perform daily physical activities and maintain independent functioning [3, 4]. Not surprisingly, adequate muscle strength has overwhelmed muscle mass as the main component of sarcopenia [5], such that a reduction in muscle strength anticipates that of muscle mass with respect to mortality rates and impaired daily living activities [6].

Among a myriad nutrition factors that may disturb muscle strength, saturated fatty acids (SFAs) can be a concern in virtue of their undisputable role in triggering systemic inflammatory pathways [7-9], thereby disturbing skeletal muscle [10]. Some observational studies have evaluated the association between dietary SFAs and muscle strength, in which inconsistencies are raised [6, 11, 12]. In older patients, dietary SFAs were not associated with muscle strength in two studies [11, 12], but one study revealed benefits of replacing dietary SFAs with polyunsaturated fatty acids on sarcopenia risk score [13].

In addition to dietary SFAs, plasma SFA levels are a noteworthy parameter in monitoring SFA status through an epidemiological manner [14-16]. However, only one study assessed such a biomarker in the context of muscle parameters, in which plasma SFA levels were associated with impaired functional capacity [17]. In this sense, the epidemiological comprehension of SFA status and muscle strength is an incipient area of research.

Interestingly, the National Health and Nutrition Examination Survey (NHANES) is a public health database that allows assessment of plasma SFAs and muscle strength in Americans [18]. In addition, NHANES contains muscle strength data through handgrip strength (HGS) [18], a pragmatic tool widely used in epidemiological and clinical settings that predicts crucial adverse outcomes (e.g., cardiometabolic diseases, disability, morbidity, and early mortality) [6]. All things considered, the aim of this study was to verify the association or the lack thereof between plasma SFA levels (total and individual types) and HGS using NHANES database.

We hypothesized that plasma total and individual types of SFA levels would be negatively associated with HGS primarily in older patients since this population is more likely to suffer from muscle strength loss than young adults due to senescence and its accompanying inflammation and oxidative stress processes [19]. Correspondingly, declines in muscle strength are slight in young and middle-aged adults while they are pronounced in older adults through an estimated loss of 15% per decade [6].

2. Methods

2.1. *Research Design*

A cross-sectional study was carried out employing data from the NHANES, 2011-2012. NHANES is an American survey developed by the National Center for Health Statistics (NCHS) that encompasses medical and nutritional data for noninstitutionalized subjects, with a multi-stage representative sample consisting of children and adults. Since NHANES cross-sectional data are public, further

information can be assessed on the Centers for Disease Control and Prevention (CDC) website.

2.2. Subjects

From 9756 subjects enrolled for NHANES 2011-2012, a subsample of 5643 subjects was collected for plasma SFA levels. A total of 1591 individuals aged 20-80 years (1106 patients <60 years; 485 patients ≥60 years) were finally included after employing the exclusion criteria: subjects aged under 20 years and no information on plasma SFAs, anthropometry, HGS and dietary data (**Figure 1**).

NHANES is a public data set and all subjects filled out written informed consent based on endorsement from the National Center for Health Statistics Research Ethics Review Board (NCHS ERB) (Protocol #2011-17 for NHANES cycle 2011-2012).

2.3. Muscle strength

Muscle strength was assessed through the sum of HGS (Takei Digital Grip Strength Dynamometer, Model T.K.K.5401), i.e., measured values from both hands. Albeit subjects capable of holding the dynamometer with one hand were tested and are available in the NHANES dataset (Muscle Strength—Grip Test data), they were excluded from our analysis as the sum of HGS was not possible.

Each subject was asked to stand and squeeze the dynamometer as hard as possible with one of the dominant or non-dominant hands, exhaling while squeezing the device to avoid increasing intrathoracic pressure. HGS test was carried out after the examiner explained and demonstrated the procedure,

adjusted the grip size of the dynamometer to the subject's hand size, and performed a practical trial on the subject. Each hand was tested three times, alternately and with one minute of rest between measurements on the same hand. Ultimately, combined HGS values were calculated in kilograms by adding the highest value of each hand.

2.4. Plasma saturated fatty acids

Blood samples were collected after an overnight fast. A 0.5-mL sample of plasma or serum was used to allow for repeated analyses, with a volume of 100 μ L per analysis. A suitable amount of plasma or serum was dispensed into a Nalge 2.0-mL cryovial or another screw-capped plastic vial labeled with sample identification and stored at -70°C.

Plasma total levels of SFAs and eleven types of SFAs were detected by using gas chromatography–spectrometry and expressed in μ mol/L. Capric acid (C10:0), lauric acid (C12:0), myristic acid (C14:0), pentadecanoic acid (C15:0), palmitic acid (C16:0), margaric acid (C17:0), stearic acid (C18:0), arachidic acid (C20:0), docosanoic acid (C22:0), tricosanoic acid (C23:0), and lignoceric acid (C24:0) were the individual types of SFAs. NHANES manual provides further information on the biochemistry assessment of plasma SFAs [18].

2.5. Dietary habits

Two 24-hour food recalls were used to assess each subject's dietary intake. The first 24-hour food recall interview was collected face-to-face and the second one was recorded by telephone three to ten days later. The average of nutrients was calculated for subjects who underwent two 24-hour food recalls.

Nutrient data for this single day were also calculated for subjects who performed only the first 24-hour food recall.

Dietary data were collected using the Automated Multiple Pass Method [20], whose method is based on a five-step multiple-pass interview approach: quick list, forgotten foods, time and occasion, detail cycle, and final probe. The USDA Food and Nutrient Database for Dietary Studies (FNDDS) 2011-2012 was used to obtain dietary items. Underlying nutrient values were derived from the USDA National Nutrient Database for Standard Reference, release 26, created by USDA's Nutrient Data Lab (<http://www.ars.usda.gov/nutrientdata>).

2.6. Statistical analysis

Plasma total SFAs and their individual types, sociodemographic data, anthropometry characteristics, physical activity, dietary habits, medical history, and lifestyle features were reported for the entire sample and according to age. Given that plasma fatty acids are obtained from an NHANES subsample, statistical analyses were performed using the "svy" command to add information concerning the "2-year fatty acid subsample" sample weight, primary sampling units, and strata for correct variance estimation.

Smoking status, annual family income, arthritis, hypertension, and diabetes were parameters not reported for the entire population in data collection, thereby we elaborated a missing category as a means of categorizing those subjects with missing values.

Linear regression analysis was used to compare the entire population and the division as per age (<60 versus ≥60 years). Continuous variables were described

as mean and standard deviation. Categorical variables were described as percentages and 95% confidence intervals.

The association of plasma total SFAs and their individual types with HGS was carried out through linear regression analysis based on crude (model 1) and adjusted (model 2) models. Regarding the latter, a fully statistical adjustment encompassed: body mass index (kg/m^2), age (years), race (non-Hispanic white, non-Hispanic black, Mexican American, other Hispanic, among other races), marital status (married or living with a partner versus widowed, divorced, separated, or never married), educational level (high school graduate or under versus some college or above), and annual family income (0 to \$19,999, \$20,000 to 54,999, 55,000 to 74,999 or over \$75,000), diabetes (pre-diabetes, yes or no), arthritis (yes or no), hypertension (presence or absence), smoking status (yes or no), physical activity level rated as moderate and vigorous exercises (yes or no), total energy (kcal/d), total protein (g/d), and alcohol (g/day).

Significant associations were adopted as p-values <0.05 . Altogether, statistical analyses were derived using Stata software version 14.0 (StataCorp, College Station, TX, USA).

3. Results

Subjects' characteristics are shown in **Table 1**, in which the data are depicted according to the entire population and age groups (<60 and ≥ 60). In general, patients aged ≥ 60 years presented low HGS as well as a lower prevalence of smoking and practice of vigorous physical activity, whereas they had a high prevalence of men, non-Hispanic white and diseases (hypertension, diabetes, pre-diabetes, and arthritis). While total plasma SFA levels did not differ between

groups, higher plasma stearic acid, margaric acid, tricosanoic acid, and arachidic acid levels were observed for those aged ≥ 60 years. Regarding dietary pattern, patients aged ≥ 60 years had a lower intake of calories and macronutrients (carbohydrates, protein, and total fat), including dietary SFAs and some unsaturated fatty acids (monounsaturated fatty acids, total polyunsaturated fatty acids, omega-3 fatty acids, and linoleic acid).

The adjusted model employed in linear regression analyses revealed no association between HGS with plasma total SFAs and their individual types in the entire sample (**Table 2**). In contrast, when subjects were divided according to age groups, there was a negative association between capric acid and stearic acid levels only for those aged < 60 years (**Table 3**).

4. Discussion

Although we hypothesized that plasma SFA levels would be negatively associated with muscle strength mainly in older patients, we observed a negative association between a couple of types of SFAs (capric acid and stearic acid) and HGS only in adults aged < 60 years.

Since dietary patterns rich in polyunsaturated fatty acids and antioxidants may be associated with higher HGS in patients aged ≥ 60 years [21], we thought that the mechanistic link of SFA-induced inflammation in myocytes (inhibition of the mTOR signaling pathway, downregulation of amino acid transporters, and elevated expression of pro-atrophic genes [22]) could affect HGS in older patients. Regardless of mechanistic interplays, the lack of association can be evident in epidemiological studies upon full adjustment models. For instance, although omega-3 fatty acids may be favorable for modulating muscle pathways

due to their anti-inflammatory and heightening skeletal muscle protein synthesis [23], a neutral association between their plasma levels and HGS for older adults was reported in another study using NHANES data [24]. That said, our data enable neutral association when viewed collectively, as the inverse association between capric acid and stearic acid levels we found does not overwhelm the lack of association between total SFA levels and the other nine individual types.

Taking into account that we assessed many types of plasma SFAs, they must be better discussed in an attempt to find a biological reasoning especially for those that achieved statistical association. SFAs can be classified according to carbon atoms: short-chain SFAs (1–6 carbons) [25], medium-chain SFAs (7–12 carbons) [25], long-chain SFAs (13–21 carbon) [26], and very long-chain SFAs (22 carbons or more) [27]. In our study, the types of SFAs negatively associated with HGS in adults aged <60 years are medium-chain and long-chain SFAs, represented by capric (C10:0) acid and stearic acid (C18:0), respectively [28].

As the main type of SFAs consumed in the United States, the intake of stearic acid (5.2 g/d for women and 8.1 g/d for men) is second only to palmitic acid (16:0), accounting for ~26% of SFA intake, 9% of total fat, and ~3% of total calories [29]. Regarding common foodstuffs, stearic acid accounts roughly for 12% of the fat content of cooked beef and pork, as well as whole milk, hard cheese, and butter [30]. Compared to red meat, white meat (e.g., skinless roast chicken breast) contains less stearic acid, representing ~8% of total fat [30]. Seemingly, chocolate is the main common food rich in stearic acid, as ~33% total fat in cocoa butter consists of stearic acid, accounting for ~33% and ~21% total fat of sweet chocolate and milk chocolate, respectively [30].

Dietary intake of capric acid is not abundant such as stearic acid, yet capric acid is present in typical foods, e.g., coconut oil, palm oil, milk, and some seeds [31-33]. Capric oil accounts for 20%–50% of medium-chain triglycerides [34, 35], whose efficacy remains unclear in the field of muscle strength and related parameters due to methodological limitations (e.g., combination with a myriad of nutrients and lack of proper dietary monitoring) [36-38] and therefore neither positive nor negative effects may be endorsed.

Similar to the dietary amount, stearic acid is the second most common SFA found in circulation, such that it is not only supplied by the diet but also endogenously synthesized from palmitic acid [25]. While circulating stearic acid levels are associated with both diet and endogenous status [25], circulating capric acid has a more exclusive relationship with diet since its endogenous synthesis is related to the mammary glands of lactating women [39].

Our results are paradoxical since plasma stearic acid levels were low in subjects aged <60 years compared with those aged ≥60 years, whereas plasma capric acid was non-statistically high (Table 1). Perhaps, such a high level of plasma stearic acid in subjects aged ≥60 years could have originated from *de novo* lipogenesis, aging-related impairment of lipid metabolism, or intrinsic pathophysiological facets as residual factors [40, 41]. Furthermore, a highly detrimental process may ensue by which stearic acid serves as a precursor to very long-chain SFAs upon elongase actions, whose high plasma levels are associated with diabetes and cardiovascular events [25]. No wonder patients aged ≥60 years had a high prevalence of diabetes, hypertension, and arthritis in our study, but we statistically adjusted the variables according to these diseases.

A couple of human studies shed light on the effect of stearic acid in triggering low-grade inflammation [42, 43]. In a three-month randomized controlled trial assessing red blood cell SFAs, stearic acid levels, but not total SFAs and palmitic acid, were positively associated with raised C-reactive protein levels (35% increase per 1 standardized deviation increment) [42]. In a randomized clinical trial of four-week isocaloric interventions, the stearic-acid diet led to higher levels of interleukin-6, tumor necrosis factor- α , and insulin resistance compared with the palmitic-acid diet [43]. Besides, patients with insulin resistance—a condition of low-grade inflammation—had higher postprandial stearic acid levels than healthy subjects [44], such that glucose load and high glycemic index loads favored this change compared to low glycemic index, whose process is mediated by the insulin-stimulated *de novo* lipogenesis in the liver via the sterol regulatory element-binding protein-1c pathway [45]. Although the majority of SFA-induced inflammation models address treatment with palmitic acid [22, 46], such an aforementioned background is noteworthy and merits further clinical attention, as a stearic acid-rich diet can be even more harmful than a palmitic acid-rich diet for the inflammatory state [43] and we observed an inverse association between HGS and plasma levels of stearic acid, but not with palmitic acid.

Additionally, in vitro studies may provide a better biological understanding of our results, mainly towards stearic acid-induced inflammation. In different cell models, treatment with stearic acid induces the production of pro-inflammatory cytokines whereby the TLR4-dependent inflammation pathway is triggered and impairs insulin action by increasing the p-JNK/JNK ratio [47, 48]. Moreover, treatment with stearic acid promotes the I κ B- α and NF- κ B expression through a

dose-dependent manner, thereby supporting the pro-inflammatory stimulus at the nuclear level [49]. Conversely, in vitro and animal studies show an anti-inflammatory potential of capric acid [50-53], thus, the inverse association between such a fatty acid in plasma with HGS we found is strikingly bearing in mind a biological reasoning. Therefore, further mechanistic studies are required to better elucidate the role of capric acid, particularly in myocytes.

A handful of studies have assessed dietary intake of SFAs and muscle strength, the association of which is unclear. In ~68,000 individuals aged ≥ 60 years from a cross-sectional analysis through the UK Biobank, dietary SFAs were not associated with HGS in either women or men [11]. In a prospective Spanish cohort addressing 1873 individuals aged ≥ 60 years whereby 331 participants developed muscle weakness during a ~5-year follow-up period, dietary SFA intake was not associated with muscle weakness measured by HGS, but was negatively associated with lower extremity functional impairment measured by the Short Physical Performance Battery (i.e., a cluster of standing balance, gait speed, and ability to rise from a chair) [12]. A cohort study of European, non-frail European men and women ($n = 986$), in turn, revealed benefits of replacing dietary SFAs with polyunsaturated fatty acids on sarcopenia risk score by combining HGS and skeletal muscle mass [13].

While the above-mentioned studies examined dietary SFA intake through questionnaires, we assessed plasma SFA levels [6, 11, 12], which can be more specific in terms of control since dietary intake is susceptible to underreporting when it is not well-controlled through a gold-standard method [54, 55]. To the best of our knowledge, only one study measured circulating SFAs in the field of muscle parameters [17]. Such a study showed that older Italians with low plasma SFA

levels were associated with a greater functional capacity of the lower limbs given by a Short Physical Performance Battery score greater than nine, whereas plasma SFA levels were associated with a longer time in the seven-meter walk test (50). Accordingly, this study assessed only functional capacity, reinforcing the importance of our findings as a means of bringing HGS as a novelty.

The pros and cons of using HGS ought to be highlighted. HGS is a non-invasive, inexpensive, easy-to-use, and portable test for assessing muscle strength [6]. HGS is even correlated with limb strength [56], however, due to its non-specificity, nuances arise as to its use for assessing global or lower limb muscle function [6].

Regarding strengths, as far as we know, this is the first study that examined the associations between circulating SFA levels and muscle mass strength. In addition, the sample size ($n = 1591$) is decent in terms of a cross-sectional design. Some limitations nevertheless can be observed. First and foremost, the cross-sectional fashion is incapable of portraying causation. Inflammation and metabolic biomarkers were not assessed, e.g., circulating cytokines, lipids and lipoproteins, C-reactive protein, fibrinogen, and insulin sensitivity; however, we adjusted the statistical model for diseases. Finally, insofar as NHANES data are a representative sample for Americans, our findings are impractical for other populations.

As for perspectives, further research is needed to reach the worldwide setting. More specifically, longitudinal studies are warranted to determine the relationship between plasma SFAs and muscle strength, such that well-controlled randomized clinical trials can help to elucidate the underlying mechanisms.

5. Conclusion

Taken together, plasma total SFAs and their types were not associated with HGS in Americans, except stearic acid and capric acid for those aged <60 years, which were inversely associated. Further research is imperative to investigate such an association in individuals suffering from major fragilities and disabilities. Likewise, randomized clinical trials are crucial to afford insights into causation and hence determine clinical effects.

Funding

None.

Author contributions

HOS wrote the manuscript; RJN, LSL, and FMSB performed statistical analysis; HOS, BBS, MEM, FMSB, and EPO participated in data description; EPO participated in the interpretation of the data and revision of the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors declare no conflicts of interest.

Acknowledgements

We thank CAPES for the financial support. EPO would like to thank The Brazilian National Council for Scientific and Technological Development (CNPq, Brazil, 304205/2019-2).

References

- [1] Rodrigues F, Domingos C, Monteiro D, Morouço P. A Review on Aging, Sarcopenia, Falls, and Resistance Training in Community-Dwelling Older Adults. *International journal of environmental research and public health*. 2022;19.
- [2] Balogun S, Winzenberg T, Wills K, Scott D, Jones G, Aitken D, et al. Prospective Associations of Low Muscle Mass and Function with 10-Year Falls Risk, Incident Fracture and Mortality in Community-Dwelling Older Adults. *The journal of nutrition, health & aging*. 2017;21:843-8.
- [3] Izquierdo M, Merchant RA, Morley JE, Anker SD, Aprahamian I, Arai H, et al. International Exercise Recommendations in Older Adults (ICFSR): Expert Consensus Guidelines. *The journal of nutrition, health & aging*. 2021;25:824-53.
- [4] Papiol M, Serra-Prat M, Vico J, Jerez N, Salvador N, Garcia M, et al. Poor Muscle Strength and Low Physical Activity Are the Most Prevalent Frailty Components in Community-Dwelling Older Adults. *Journal of aging and physical activity*. 2016;24:363-8.
- [5] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age and ageing*. 2019;48:16-31.
- [6] Tatangelo T, Muollo V, Ghiotto L, Schena F, Rossi AP. Exploring the association between handgrip, lower limb muscle strength, and physical function in older adults: A narrative review. *Experimental gerontology*. 2022;167:111902.
- [7] Huang S, Rutkowski JM, Snodgrass RG, Ono-Moore KD, Schneider DA, Newman JW, et al. Saturated fatty acids activate TLR-mediated proinflammatory signaling pathways. *Journal of lipid research*. 2012;53:2002-13.
- [8] Fritsche KL. The science of fatty acids and inflammation. *Advances in nutrition (Bethesda, Md)*. 2015;6:293s-301s.
- [9] Håversen L, Danielsson KN, Fogelstrand L, Wiklund O. Induction of proinflammatory cytokines by long-chain saturated fatty acids in human macrophages. *Atherosclerosis*. 2009;202:382-93.
- [10] Pillon NJ, Arane K, Bilan PJ, Chiu TT, Klip A. Muscle cells challenged with saturated fatty acids mount an autonomous inflammatory response that activates macrophages. *Cell communication and signaling : CCS*. 2012;10:30.
- [11] Gedmantaitė A, Celis-Morales CA, Ho F, Pell JP, Ratkevicius A, Gray SR. Associations between diet and handgrip strength: a cross-sectional study from UK Biobank. *Mechanisms of ageing and development*. 2020;189:111269.
- [12] Arias-Fernández L, Struijk EA, Rodríguez-Artalejo F, Lopez-Garcia E, Lana A. Habitual dietary fat intake and risk of muscle weakness and lower-extremity functional impairment in older adults: A prospective cohort study. *Clinical nutrition (Edinburgh, Scotland)*. 2020;39:3663-70.
- [13] Montiel-Rojas D, Santoro A, Nilsson A, Franceschi C, Capri M, Bazzocchi A, et al. Beneficial Role of Replacing Dietary Saturated Fatty Acids with Polyunsaturated Fatty Acids in the Prevention of Sarcopenia: Findings from the NU-AGE Cohort. *Nutrients*. 2020;12.
- [14] Lemaitre RN, Fretts AM, Sitlani CM, Biggs ML, Mukamal K, King IB, et al. Plasma phospholipid very-long-chain saturated fatty acids and incident diabetes in older adults: the Cardiovascular Health Study. *The American journal of clinical nutrition*. 2015;101:1047-54.
- [15] Zheng JS, Sharp SJ, Imamura F, Koulman A, Schulze MB, Ye Z, et al. Association between plasma phospholipid saturated fatty acids and metabolic markers of lipid, hepatic, inflammation and glycaemic pathways in eight European countries: a cross-sectional analysis in the EPIC-InterAct study. *BMC medicine*. 2017;15:203.
- [16] Harris K, Oshima M, Sattar N, Würtz P, Jun M, Welsh P, et al. Plasma fatty acids and the risk of vascular disease and mortality outcomes in individuals with type 2 diabetes: results from the ADVANCE study. *Diabetologia*. 2020;63:1637-47.

- [17] Abbatecola AM, Cherubini A, Guralnik JM, Andres Lacueva C, Ruggiero C, Maggio M, et al. Plasma polyunsaturated fatty acids and age-related physical performance decline. *Rejuvenation research*. 2009;12:25-32.
- [18] NHANES. Laboratory Procedure Manual. 2011.
- [19] Wilkinson DJ, Piasecki M, Atherton PJ. The age-related loss of skeletal muscle mass and function: Measurement and physiology of muscle fibre atrophy and muscle fibre loss in humans. *Ageing research reviews*. 2018;47:123-32.
- [20] Moshfegh AJ, Rhodes DG, Baer DJ, Murayi T, Clemens JC, Rumpler WV, et al. The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *The American journal of clinical nutrition*. 2008;88:324-32.
- [21] Tak YJ, Lee JG, Yi YH, Kim YJ, Lee S, Cho BM, et al. Association of Handgrip Strength with Dietary Intake in the Korean Population: Findings Based on the Seventh Korea National Health and Nutrition Examination Survey (KNHANES VII-1), 2016. *Nutrients*. 2018;10.
- [22] Lipina C, Hundal HS. Lipid modulation of skeletal muscle mass and function. *Journal of cachexia, sarcopenia and muscle*. 2017;8:190-201.
- [23] Ferguson EJ, Seigel JW, McGlory C. Omega-3 fatty acids and human skeletal muscle. *Current opinion in clinical nutrition and metabolic care*. 2021;24:114-9.
- [24] Batista RAB, de Branco FMS, Nehme R, de Oliveira EP, Pena GDG. Association between Plasma Omega-3 and Handgrip Strength According to Glycohemoglobin Levels in Older Adults: Results from NHANES 2011-2012. *Nutrients*. 2022;14.
- [25] Schönfeld P, Wojtczak L. Short- and medium-chain fatty acids in energy metabolism: the cellular perspective. *Journal of lipid research*. 2016;57:943-54.
- [26] Hidalgo MA, Carretta MD, Burgos RA. Long Chain Fatty Acids as Modulators of Immune Cells Function: Contribution of FFA1 and FFA4 Receptors. *Frontiers in physiology*. 2021;12:668330.
- [27] Kihara A. Very long-chain fatty acids: elongation, physiology and related disorders. *Journal of biochemistry*. 2012;152:387-95.
- [28] Lyudinina AY, Ivankova GE, Bojko ER. Priority use of medium-chain fatty acids during high-intensity exercise in cross-country skiers. *Journal of the International Society of Sports Nutrition*. 2018;15:57.
- [29] Kris-Etherton PM, Griel AE, Psota TL, Gebauer SK, Zhang J, Etherton TD. Dietary stearic acid and risk of cardiovascular disease: intake, sources, digestion, and absorption. *Lipids*. 2005;40:1193-200.
- [30] U.S. Department of Agriculture, Agricultural Research Service. FoodData Central, 2019. fdc.nal.usda.gov.
- [31] Jadhav HB, Annapure US. Triglycerides of medium-chain fatty acids: a concise review. *Journal of food science and technology*. 2023;60:2143-52.
- [32] Santos HO, Howell S, Earnest CP, Teixeira FJ. Coconut oil intake and its effects on the cardiometabolic profile - A structured literature review. *Progress in cardiovascular diseases*. 2019;62:436-43.
- [33] Shekhar N, Tyagi S, Rani S, Thakur AK. Potential of Capric Acid in Neurological Disorders: An Overview. *Neurochemical research*. 2023;48:697-712.
- [34] McCarty MF, DiNicolantonio JJ. Lauric acid-rich medium-chain triglycerides can substitute for other oils in cooking applications and may have limited pathogenicity. *Open heart*. 2016;3:e000467.
- [35] Lemarié F, Beauchamp E, Legrand P, Rioux V. Revisiting the metabolism and physiological functions of caprylic acid (C8:0) with special focus on ghrelin octanoylation. *Biochimie*. 2016;120:40-8.
- [36] St-Onge MP, Bosarge A. Weight-loss diet that includes consumption of medium-chain triacylglycerol oil leads to a greater rate of weight and fat mass loss than does olive oil. *The American journal of clinical nutrition*. 2008;87:621-6.

- [37] Abe S, Ezaki O, Suzuki M. Medium-chain triglycerides (8:0 and 10:0) are promising nutrients for sarcopenia: a randomized controlled trial. *The American journal of clinical nutrition*. 2019;110:652-65.
- [38] Abe S, Ezaki O, Suzuki M. Medium-Chain Triglycerides in Combination with Leucine and Vitamin D Increase Muscle Strength and Function in Frail Elderly Adults in a Randomized Controlled Trial. *The Journal of nutrition*. 2016;146:1017-26.
- [39] Hachey DL, Silber GH, Wong WW, Garza C. Human lactation. II: Endogenous fatty acid synthesis by the mammary gland. *Pediatric research*. 1989;25:63-8.
- [40] Lelliott C, Vidal-Puig AJ. Lipotoxicity, an imbalance between lipogenesis de novo and fatty acid oxidation. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity*. 2004;28 Suppl 4:S22-8.
- [41] Zhu Y, Vogelpohl FA, Heiner-Fokkema MR, Pranger IG, Minović I, Navis GJ, et al. Circulating de novo lipogenesis fatty acids and all-cause mortality in a prospective Dutch population cohort. *Journal of clinical lipidology*. 2022;16:658-66.
- [42] Mu L, Mukamal KJ, Naqvi AZ. Erythrocyte saturated fatty acids and systemic inflammation in adults. *Nutrition (Burbank, Los Angeles County, Calif)*. 2014;30:1404-8.
- [43] van Rooijen MA, Plat J, Blom WAM, Zock PL, Mensink RP. Dietary stearic acid and palmitic acid do not differently affect ABCA1-mediated cholesterol efflux capacity in healthy men and postmenopausal women: A randomized controlled trial. *Clinical nutrition (Edinburgh, Scotland)*. 2021;40:804-11.
- [44] Liu L, Chu X, Na L, Yuan F, Li Y, Sun C. Decreasing high postprandial stearic acid in impaired fasting glucose by dietary regulation. *European journal of clinical nutrition*. 2016;70:795-801.
- [45] Chu X, Liu L, Na L, Lu H, Li S, Li Y, et al. Sterol regulatory element-binding protein-1c mediates increase of postprandial stearic acid, a potential target for improving insulin resistance, in hyperlipidemia. *Diabetes*. 2013;62:561-71.
- [46] Korbecki J, Bajdak-Rusinek K. The effect of palmitic acid on inflammatory response in macrophages: an overview of molecular mechanisms. *Inflammation research : official journal of the European Histamine Research Society [et al]*. 2019;68:915-32.
- [47] Miao H, Chen L, Hao L, Zhang X, Chen Y, Ruan Z, et al. Stearic acid induces proinflammatory cytokine production partly through activation of lactate-HIF1 α pathway in chondrocytes. *Scientific reports*. 2015;5:13092.
- [48] Wang S, Xiang N, Yang L, Zhu C, Zhu X, Wang L, et al. Linoleic acid and stearic acid elicit opposite effects on AgRP expression and secretion via TLR4-dependent signaling pathways in immortalized hypothalamic N38 cells. *Biochemical and biophysical research communications*. 2016;471:566-71.
- [49] Harvey KA, Walker CL, Pavlina TM, Xu Z, Zaloga GP, Siddiqui RA. Long-chain saturated fatty acids induce pro-inflammatory responses and impact endothelial cell growth. *Clinical nutrition (Edinburgh, Scotland)*. 2010;29:492-500.
- [50] Park EJ, Kim SA, Choi YM, Kwon HK, Shim W, Lee G, et al. Capric acid inhibits NO production and STAT3 activation during LPS-induced osteoclastogenesis. *PloS one*. 2011;6:e27739.
- [51] Walker ME, Matthan NR, Goldbaum A, Meng H, Lamon-Fava S, Lakshman S, et al. Dietary patterns influence epicardial adipose tissue fatty acid composition and inflammatory gene expression in the Ossabaw pig. *The Journal of nutritional biochemistry*. 2019;70:138-46.
- [52] Martínez-Galán JP, Ontibón-Echeverri CM, Campos Costa M, Batista-Duharte A, Guerso Batista V, Mesa V, et al. Enzymatic synthesis of capric acid-rich structured lipids and their effects on mice with high-fat diet-induced obesity. *Food research international (Ottawa, Ont)*. 2021;148:110602.
- [53] Lee SI, Kang KS. Function of capric acid in cyclophosphamide-induced intestinal inflammation, oxidative stress, and barrier function in pigs. *Scientific reports*. 2017;7:16530.
- [54] Waterworth SP, Kerr CJ, McManus CJ, Costello R, Sandercock GRH. Obese individuals do not underreport dietary intake to a greater extent than nonobese individuals when data are

allometrically-scaled. American journal of human biology : the official journal of the Human Biology Council. 2022;34:e23743.

[55] Macdiarmid J, Blundell J. Assessing dietary intake: Who, what and why of under-reporting. Nutrition research reviews. 1998;11:231-53.

[56] Strandkvist V, Larsson A, Pauelsen M, Nyberg L, Vikman I, Lindberg A, et al. Hand grip strength is strongly associated with lower limb strength but only weakly with postural control in community-dwelling older adults. Archives of gerontology and geriatrics. 2021;94:104345.

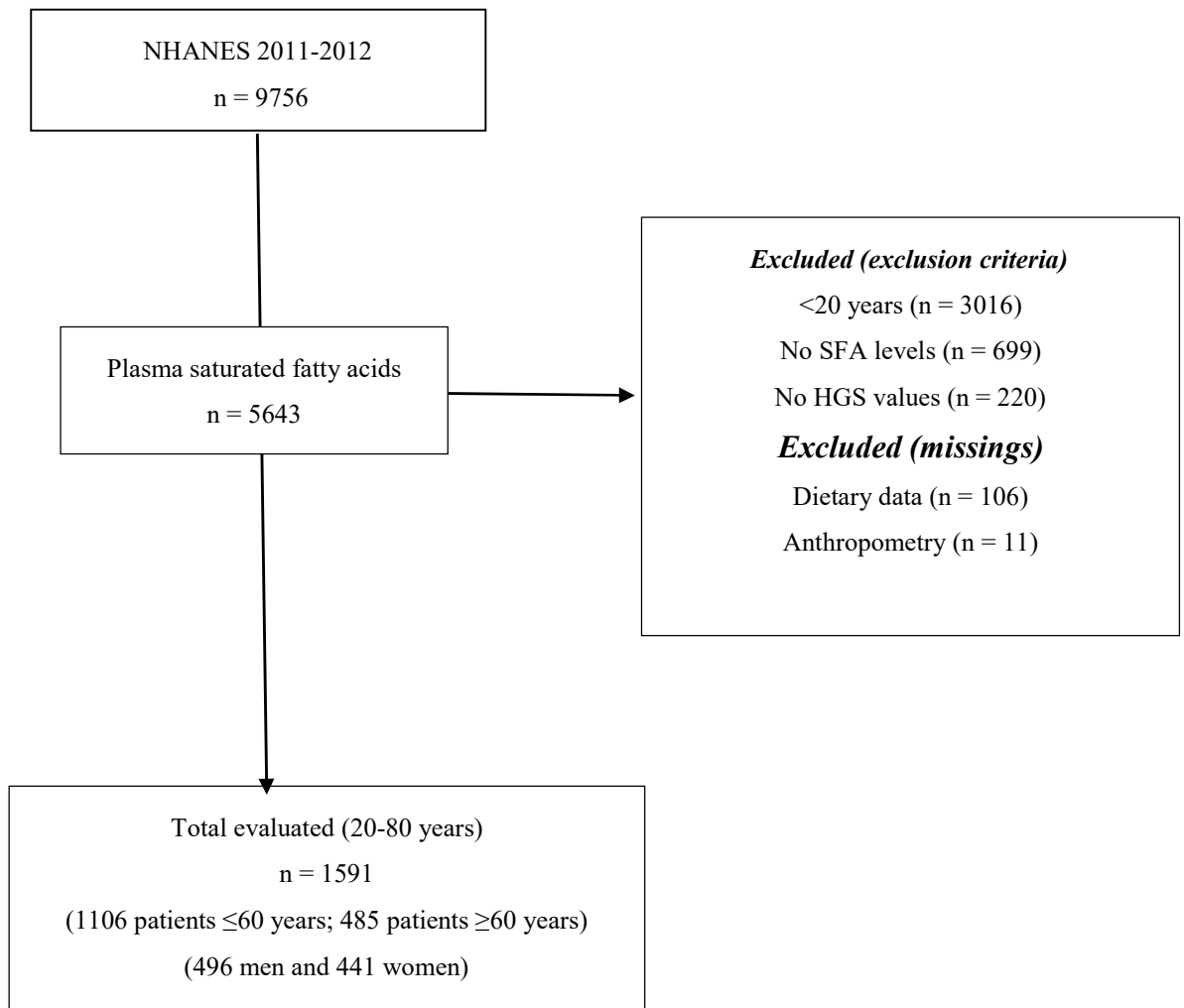


Figure 1. Flowchart of the sample selection from NHANES (2011-2012).
HGS, handgrip strength; SFA, saturated fatty acid.

Table 1. Sociodemographic, anthropometric, and dietary characteristics the in total sample and according to age. Data from NHANES (2011-2012).

Variables	Total	<60 years	≥60 years	p-Value
<i>Sociodemographic Characteristics</i>				
Age, y	47.2 ± 16.8	39.4 ± 11.6	69 ± 6.8	<0.001
Sex, %				0.023
Women	48 (45; 51.1)	49.6 (45.7; 53.5)	43.5 (40.2; 47)	
Men	52 (48.9; 55)	50.4 (46.5; 54.3)	56.5 (53; 59.8)	
Race/ethnicity, %				<0.001
Non-Hispanic White	69.11 (60.4; 76.6)	64.6 (55.4; 72.9)	81.6 (74.6; 87.1)	
Others (Mexican American, Other Hispanic, Non-Hispanic Black, and Multi-Racial)	30.9 (23.4; 39.6)	35.4 (23.1; 44.6)	18.4 (12.9; 25.4)	
Marital status, %				0.020
Married/Living with Partner	63 (58; 67.7)	60.3 (54.3; 66)	2.9 (76.2; 0)	
Single/Divorced/Widowed/Never Married	37 (32.3; 42)	39.7 (34; 45.7)	29.6 (23.8; 36.1)	
Annual Family Income, %				0.217
\$0-19,999	18.1 (14.3; 22.6)	19.3 (14.6; 25)	14.8 (10.2; 21)	
\$20,000-54,999	36.2 (31.1; 41.7)	33.5 (28.3; 39.1)	43.8 (33.8; 54.4)	
Over \$55,000	12.2 (9.1; 16.1)	11.4 (8.8; 14.7)	14.3 (7.5; 25.5)	
Over \$75,000	30.6 (24.3; 37.8)	32.9 (26.9; 39.6)	24.2 (13.9; 38.7)	
Missing	2.9 (2; 4.2)	2.9 (1.9; 4.3)	2.8 (1.5; 5.5)	
Educational level, %				0.033
Under high school graduate	34.9 (29; 41.3)	32.5 (26.5; 39.2)	41.5 (32.8; 50.8)	
Some college or over	65.1 (58.7; 71)	67.5 (60.8; 73.5)	58.5 (49.2; 67.2)	
<i>Health Conditions and Behavior</i>				
Hypertension, %				<0.001
No	66.8 (62.1; 71.2)	76 (71.5; 79.9)	41.3 (33.6; 49.5)	
Yes	33.2 (28.8; 37.9)	24 (20; 28.5)	58.7 (50.5; 66.4)	

Missing	0 (0; 0.2)	0 (0; 0.2)	0 (0; 0)	
Diabetes, %				<0.001
No	89 (86.8; 90.9)	93.3 (91.5; 94.8)	77.1 (72.1; 81.5)	
Yes	9 (7.1; 11.3)	5.6 (4.1; 7.6)	18.5 (13.5; 24.8)	
Pre-diabetes	1.9 (1; 3.8)	1.1 (0.3; 4.2)	4.4 (2.2; 8.4)	
Missing	0 (0; 0.2)	0 (0; 0.4)	0 (0; 0.4)	
Arthritis, %				<0.001
No	76.2 (72.7; 79.4)	84.5 (81.7; 86.8)	53.2 (46.2; 60)	
Yes	23.7 (20.5; 27.2)	15.5 (13.2; 18.3)	46.3 (39.4; 53.3)	
Missing	0.1 (0.1; 0.2)	0 (0; 0)	0.6 (0.4; 0.8)	
Smoking status, %				0.001
No	80.2 (76.1; 83.8)	77.4 (72.9; 81.4)	88 (82.2; 92.1)	
Yes	19.7 (16.1; 23.9)	22.5 (18.6; 27)	11.9 (7.8; 17.7)	
Missing	0.1 (0; 0.3)	0.1 (0; 0.4)	0.1 (0; 0.5)	
Vigorous Physical Activity, %				<0.001
Yes	19.1 (16.1; 22.6)	22.3 (18.4; 26.7)	10.2 (7; 14.6)	
No	80.9 (77.4; 83.9)	77.7 (73.3; 81.6)	89.8 (85.4; 93)	
Moderate Physical Activity, %				0.161
Yes	39 (35; 43.3)	40.7 (36.4; 45.2)	34.3 (26.4; 43.2)	
No	61 (56.7; 65)	59.3 (54.8; 63.6)	65.7 (56.8; 73.6)	
<i>Anthropometric Characteristics and Strength</i>				
Body Mass, kg	82.5 ± 21	83.2 ± 21.7	80.4 ± 18.9	0.126
Height, m	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	<0.001
Body mass index, kg/m ²	28.7 ± 6.5	28.6 ± 6.7	28.9 ± 5.9	0.581
Sum of handgrip strength, kg	72.5 ± 22.5	76.7 ± 22.1	60.7 ± 19	<0.001
<i>Plasma fatty acids</i>				
Total saturated fatty acids, µmol/L	4093.2 ± 1386.8	4074.1 ± 1438.6	4146.4 ± 1231.2	0.385
Lauric acid, µmol/L	13.8 ± 20.9	13.9 ± 22	13.5 ± 17.4	0.779

Palmitic acid, $\mu\text{mol/L}$	2986.6 $\pm$ 1076	2975.7 $\pm$ 1117.2	3017 $\pm$ 952.7	0.556
Capric acid, $\mu\text{mol/L}$	2.9 $\pm$ 5	3 $\pm$ 5.4	2.6 $\pm$ 3.5	0.128
Stearic acid, $\mu\text{mol/L}$	707.6 $\pm$ 197.6	700.2 $\pm$ 202.7	728 $\pm$ 181.2	0.004
Margaric acid, $\mu\text{mol/L}$	32 $\pm$ 9.6	31.6 $\pm$ 9.5	33.2 $\pm$ 9.6	0.008
Pentadecanoic acid, $\mu\text{mol/L}$	25.4 $\pm$ 11	25.4 $\pm$ 11.1	25.6 $\pm$ 10.7	0.756
Arachidic acid, $\mu\text{mol/L}$	24.1 $\pm$ 5.7	23.8 $\pm$ 5.6	24.9 $\pm$ 5.7	0.005
Tricosanoic acid, $\mu\text{mol/L}$	29.4 $\pm$ 7.5	29.1 $\pm$ 7.4	30.2 $\pm$ 7.8	0.010
Lignoceric acid, $\mu\text{mol/L}$	59 $\pm$ 14.5	58.5 $\pm$ 13.9	60.2 $\pm$ 16.1	0.257
Docosanoic acid, $\mu\text{mol/L}$	69.2 $\pm$ 17.2	68.6 $\pm$ 16.6	70.9 $\pm$ 18.6	0.081
Myristic acid, $\mu\text{mol/L}$	143.2 $\pm$ 103.1	144.3 $\pm$ 106.9	140.3 $\pm$ 91.7	0.549
Dietary Intake				
Energy, kcal/d	2112.4 $\pm$ 818.9	2215 $\pm$ 854	1826.4 $\pm$ 629.9	<0.001
Carbohydrate, g/d	256.7 $\pm$ 105.7	269.6 $\pm$ 108.4	220.5 $\pm$ 88.2	<0.001
Protein, g/d	82.6 $\pm$ 35.2	86 $\pm$ 37	73.3 $\pm$ 27.6	<0.001
Protein, g/kg	1.0 $\pm$ 0.5	1.1 $\pm$ 0.5	0.9 $\pm$ 0.4	<0.001
Total fat, g/d	79.6 $\pm$ 37.9	83.1 $\pm$ 39.7	69.9 $\pm$ 30.0	<0.001
Saturated fatty acids, g/d	25.7 $\pm$ 13.3	26.9 $\pm$ 13.9	22.2 $\pm$ 10.7	<0.001
Monounsaturated fats, g/d	28.4 $\pm$ 14.4	29.5 $\pm$ 15	25.1 $\pm$ 11.9	0.001
Polyunsaturated fatty acids, g/d	19 $\pm$ 10.3	19.7 $\pm$ 10.9	17.1 $\pm$ 8.4	0.002
Omega-3 polyunsaturated fatty acids, g/d	383.2 $\pm$ 177.8	358.4 $\pm$ 152	452.7 $\pm$ 221.3	<0.001
Alpha-linolenic acid, g/d	1.8 $\pm$ 1.1	1.8 $\pm$ 1.1	1.7 $\pm$ 1.0	0.090
Eicosapentaenoic acid, g/d	0 $\pm$ 0.1	0 $\pm$ 0.1	0 $\pm$ 0.1	0.574
Docosahexaenoic acid, g/d	0.1 $\pm$ 0.1	0.1 $\pm$ 0.1	0.1 $\pm$ 0.1	0.682
Linoleic acid, g/d	16.8 $\pm$ 9.3	17.4 $\pm$ 9.8	15 $\pm$ 7.5	0.001
Total fiber (g/d)	18 $\pm$ 9.9	18.3 $\pm$ 9.5	17.2 $\pm$ 11	0.296
Alcohol, g/d	9.7 $\pm$ 21.7	10.5 $\pm$ 23.1	7.4 $\pm$ 16.9	0.058

Data are described as mean (standard deviation) or percentage (confidence interval).

Table 2. Linear regression between muscle strength with plasma total SFAs and their individual types in all patients regardless of age. Results from NHANES (2011-2012).

Model 1: crude analysis. Model 2: each variable was adjusted for energy intake, protein intake, smoking, family income,

	Model 1		Model 2	
Plasma fatty acids	β (95%CI)	<i>p</i> -value	β (95%CI)	<i>p</i> -value
Saturated total	0.0002 (-0.0006; 0.0010)	0.579	0.0000 (-0.0006; 0.0008)	0.795
Lauric acid	-0.0060 (0.0600; 0.0500)	0.825	-0.0200 (-0.0700; 0.0200)	0.395
Palmitic acid	0.0005 (-0.0004; 0.0015)	0.252	0.0001 (-0.0007; 0.0010)	0.735
Capric acid	0.1000 (-0.1466; 0.3429)	0.409	-0.2278 (-0.5005; 0.0400)	0.096
Stearic acid	-0.0052 (- 0.0100; 0.0016)	0.126	0.0002 (- 0.0046; 0.0052)	0.901
Margaric acid	-0.0200 (0.1542; 0.1145)	0.759	0.0041 (-0.1000; 0.1064)	0.933
Pentadecanoic acid	-0.0500 (0.1856; 0.0900)	0.488	-0.1000 (-0.1267; 0.1000)	0.801
Arachidic acid	-0.8140 (-1.072; 0.5558)	0.000	0.0300 (-0.1166; 0.1700)	0.699
Tricosanoic acid	-0.7082 (-0.8878; 0.5286)	0.000	0.0300 (-0.0900; 0.1444)	0.624
Lignoceric acid	-0.0500 (0.1531; 0.0500)	0.291	0.0300 (-0.0200; 0.0900)	0.215
Docosanoic acid	-0.1635 (0.2482; 0.0800)	0.001	0.0400 (-0.0071; 0.8000)	0.097
Myristic acid				

diabetes, arterial hypertension, alcohol, marital status, education level, arthritis, body mass index (kg/m²), physical activity, age, sex, and race. Data are shown as coefficients. and 95% confidence intervals (95% CI). P-values < 0.05 were considered statistically significant.

Table 3. Linear regression between muscle strength with plasma total SFAs and their individual types according to age (<60 years and ≥60 years). Results from NHANES (2011-2012).

	Patients with <60 years				Patients with ≥60 years			
	Model 1		Model 2		Model 1		Model 2	
Plasma fatty acids	β (95%CI)	<i>p</i> -value	β (95%CI)	<i>p</i> -value	β (95%CI)	<i>p</i> -value	β (95%CI)	<i>p</i> -value
Saturated, total	0.0005 (-0.0000; 0.0011)	0.083	-0.0006 (-0.0014; 0.0000)	0.068	-0.0004 (-0.0043; 0.0034)	0.800	0.013 (-0.0003; 0.0031)	0.119
Lauric Acid	-0.0081 (-0.0500; 0.0300)	0.720	-0.0400 (-0.0900; 0.0100)	0.130	-0.0200 (-0.2059; 0.1767)	0.874	0.0400 (-0.0800; 0.1511)	0.512
Palmitic acid	0.0009 (0.0000; 0.0018)	0.033	-0.0007 (-0.0017; 0.0001)	0.083	-0.0003 (-0.0053; 0.0046)	0.890	0.0018 (-0.0005; 0.0041)	0.119
Capric acid	0.0300 (-0.2259; 0.2998)	0.771	-0.2978 (-0.5855; -0.0100)	0.043	0.1190 (-0.8763; 1.1143)	0.804	0.1302 (-0.3090; 0.5695)	0.540
Stearic acid	-0.0007 (-0.058; 0.0043)	0.765	-0.0058 (-0.0100; -0.0003)	0.038	-0.0100 (-0.0300; 0.0100)	0.317	0.0083 (-0.0011; 0.0200)	0.081
Margaric acid	0.1260 (0.0061; 0.2460)	0.040	-0.0700 (-0.1635; 0.0300)	0.142	-0.2129 (-0.6290; 0.2030)	0.295	0.1000 (-0.1094; 0.3024)	0.337
Pentadecanoic acid	-0.3000 (-0.1189; 0.0600)	0.507	-0.0900 (-0.1956; 0.0200)	0.099	-0.0800 (-0.5003; 0.3434)	0.700	0.1375 (-0.0800; 0.3542)	0.198
Arachidic acid	-0.6508 (-0.9544; -0.3472)	0.000	-0.1422 (-0.3380; 0.0500)	0.144	-0.8550 (-1.3133; -0.3967)	0.001	0.0500 (-0.1893; 0.2985)	0.634
Tricosanoic acid	-0.6700 (-0.8720; -0.4680)	0.000	-0.1145 (-0.2410; 0.0100)	0.073	-0.5983 (-0.9154; -0.2812)	0.001	0.0400 (-0.1720; 0.2462)	0.713
Lignoceric acid	-0.0033 (-0.1185; 0.1117)	0.951	-0.0500 (-0.1203; 0.0300)	0.220	-0.0700 (-0.2583; 0.1086)	0.401	0.0300 (-0.0600; 0.1328)	0.466
Docosanoic acid	-0.1434 (-0.2401; -0.0500)	0.006	-0.0300 (-0.0900; 0.0400)	0.402	-0.1317 (-0.2888; 0.0200)	0.095	0.0500 (-0.0500; 0.1418)	0.308
Myristic acid	0.0082 (-0.0040; 0.0200)	0.174	-0.0089 (-0.0200; 0.0029)	0.131	0.0100 (-0.0500; 0.0700)	0.682	0.0200 (-0.0100; 0.0500)	0.250

Model 1: crude analysis. Model 2: each variable was adjusted for energy intake, protein intake, smoking, family income, diabetes, arterial hypertension, alcohol, marital status, education level, arthritis, body mass index (kg/m²), physical activity, age, sex, and race. Data are shown as coefficients. and 95% confidence intervals (95% CI). P-values < 0.05 were considered statistically significant.

5. CONCLUSÃO

Apesar dos mecanismos pró-inflamatórios dos AGS no músculo esquelético, os AGS plasmáticos totais e seus subtipos não associaram com o IMMA e força muscular em norte-americanos, no geral. Observou-se, apenas, associação inversa para força muscular com ácido esteárico e ácido cáprico para aqueles com idade <60 anos, a qual não se sobressai em relação à falta de associação como um todo.

6. PERSPECTIVAS

É primordial desenvolver estudos longitudinais para determinar a relação entre os AGS plasmáticos e a força muscular no longo prazo. Igualmente, a condução de ensaios clínicos randomizados bem controlados é frutífera, podendo elucidar os mecanismos subjacentes através do padrão-ouro de desenho de estudo.

7. PÓS-TEXTO – REFERÊNCIAS

ABBATECOLA, A. M.; CHERUBINI, A.; GURALNIK, J. M.; ANDRES LACUEVA, C. et al. Plasma polyunsaturated fatty acids and age-related physical performance decline. *Rejuvenation Res*, 12, n. 1, p. 25-32, Feb 2009.

<https://doi.org/10.1089/rej.2008.0799>

ABRAMOWITZ, M. K.; HALL, C. B.; AMODU, A.; SHARMA, D. et al. Muscle mass, BMI, and mortality among adults in the United States: A population-based cohort study. *PLoS One*, 13, n. 4, p. e0194697, 2018.

<https://doi.org/10.1371/journal.pone.0194697>

ARIAS-FERNÁNDEZ, L.; STRUIJK, E. A.; RODRÍGUEZ-ARTEALEJO, F.; LOPEZ-GARCIA, E. et al. Habitual dietary fat intake and risk of muscle weakness and lower-extremity functional impairment in older adults: A prospective cohort study. *Clin Nutr*, 39, n. 12, p. 3663-3670, Dec 2020.

<https://doi.org/10.1016/j.clnu.2020.03.018>

ASP, M. L.; RICHARDSON, J. R.; COLLENE, A. L.; DROLL, K. R. et al. Dietary protein and beef consumption predict for markers of muscle mass and nutrition status in older adults. *J Nutr Health Aging*, 16, n. 9, p. 784-790, 2012.

<https://doi.org/10.1007/s12603-012-0064-6>

BALOGUN, S.; WINZENBERG, T.; WILLS, K.; SCOTT, D. et al. Prospective Associations of Low Muscle Mass and Function with 10-Year Falls Risk, Incident Fracture and Mortality in Community-Dwelling Older Adults. *J Nutr Health Aging*, 21, n. 7, p. 843-848, 2017.

<https://doi.org/10.1007/s12603-016-0843-6>

BEASLEY, J. M.; SHIKANY, J. M.; THOMSON, C. A. The role of dietary protein intake in the prevention of sarcopenia of aging. *Nutr Clin Pract*, 28, n. 6, p. 684-690, Dec 2013.

<https://doi.org/10.1177/0884533613507607>

BOKSHAN, S. L.; DEPASSE, J. M.; DANIELS, A. H. Sarcopenia in Orthopedic Surgery. *Orthopedics*, 39, n. 2, p. e295-300, Mar-Apr 2016.

<https://doi.org/10.3928/01477447-20160222-02>

BUSCEMI, C.; FERRO, Y.; PUJIA, R.; MAZZA, E. et al. Sarcopenia and Appendicular Muscle Mass as Predictors of Impaired Fasting Glucose/Type 2 Diabetes in Elderly Women. *Nutrients*, 13, n. 6, Jun 2 2021.

<https://doi.org/10.3390/nu13061909>

CESARI, M.; PAHOR, M.; BARTALI, B.; CHERUBINI, A. et al. Antioxidants and physical performance in elderly persons: the Invecchiare in Chianti (InCHIANTI) study. *Am J Clin Nutr*, 79, n. 2, p. 289-294, Feb 2004.

<https://doi.org/10.1093/ajcn/79.2.289>

CHAI, W.; MORIMOTO, Y.; COONEY, R. V.; FRANKE, A. A. et al. Dietary Red and Processed Meat Intake and Markers of Adiposity and Inflammation: The Multiethnic Cohort Study. *J Am Coll Nutr*, 36, n. 5, p. 378-385, Jul 2017.

<https://doi.org/10.1080/07315724.2017.1318317>

CHEN, L.; SHIVAPPA, N.; DONG, X.; MING, J. et al. Association between appendicular skeletal muscle index and leukocyte telomere length in adults: A study from National Health and Nutrition Examination Survey (NHANES) 1999-2002. *Clin Nutr*, 40, n. 5, p. 3470-3478, May 2021.

<https://doi.org/10.1016/j.clnu.2020.11.031>

CLARYS, J. P.; MARTIN, A. D.; MARFELL-JONES, M. J.; JANSSENS, V. et al. Human body composition: A review of adult dissection data. *Am J Hum Biol*, 11, n. 2, p. 167-174, 1999.

[https://doi.org/10.1002/\(SICI\)1520-6300\(1999\)11:2<167::AID-AJHB4>3.0.CO;2-G](https://doi.org/10.1002/(SICI)1520-6300(1999)11:2<167::AID-AJHB4>3.0.CO;2-G)

COLL, P. P.; PHU, S.; HAJJAR, S. H.; KIRK, B. et al. The prevention of osteoporosis and sarcopenia in older adults. *J Am Geriatr Soc*, 69, n. 5, p. 1388-1398, May 2021.

<https://doi.org/10.1111/jgs.17043>

CRUZ-JENTOFT, A. J.; BAHAT, G.; BAUER, J.; BOIRIE, Y. et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*, 48, n. 1, p. 16-31, Jan 1 2019.

<https://doi.org/10.1093/ageing/afz046>

DALY, R. M.; O'CONNELL, S. L.; MUNDELL, N. L.; GRIMES, C. A. et al. Protein-enriched diet, with the use of lean red meat, combined with progressive resistance training enhances lean tissue mass and muscle strength and reduces circulating IL-6 concentrations in elderly women: a cluster randomized controlled trial. *Am J Clin Nutr*, 99, n. 4, p. 899-910, Apr 2014.

<https://doi.org/10.3945/ajcn.113.064154>

DANIEL, C. R.; CROSS, A. J.; KOEBNICK, C.; SINHA, R. Trends in meat consumption in the USA. *Public Health Nutr*, 14, n. 4, p. 575-583, Apr 2011.

<https://doi.org/10.1017/S1368980010002077>

DE BRANCO, F. M. S.; ROSSATO, L. T.; RINALDI, A. E. M.; AZEREDO, C. M. et al. Plasma omega-3 is not associated with appendicular muscle mass index in young and middle-aged individuals: Results from NHANES 2011-2012. *Prostaglandins Leukot Essent Fatty Acids*, 178, p. 102412, Mar 2022.

<https://doi.org/10.1016/j.plefa.2022.102412>

DE SANTANA, F. M.; PREMAOR, M. O.; TANIGAVA, N. Y.; PEREIRA, R. M. R. Low muscle mass in older adults and mortality: A systematic review and meta-analysis. *Exp Gerontol*, 152, p. 111461, Sep 2021.

<https://doi.org/10.1016/j.exger.2021.111461>

FERNANDEZ, M. L.; WEST, K. L. Mechanisms by which dietary fatty acids modulate plasma lipids. *J Nutr*, 135, n. 9, p. 2075-2078, Sep 2005.

<https://doi.org/10.1093/jn/135.9.2075>

FRITSCHKE, K. L. The science of fatty acids and inflammation. *Adv Nutr*, 6, n. 3, p. 293s-301s, May 2015.

<https://doi.org/10.3945/an.114.006940>

GEDMANTAITE, A.; CELIS-MORALES, C. A.; HO, F.; PELL, J. P. et al. Associations between diet and handgrip strength: a cross-sectional study from UK Biobank. *Mech Ageing Dev*, 189, p. 111269, Jul 2020.

<https://doi.org/10.1016/j.mad.2020.111269>

GRANIC, A.; JAGGER, C.; DAVIES, K.; ADAMSON, A. et al. Effect of Dietary Patterns on Muscle Strength and Physical Performance in the Very Old: Findings from the Newcastle 85+ Study. PLoS One, 11, n. 3, p. e0149699, 2016.

<https://doi.org/10.1371/journal.pone.0149699>

GREENBERG, J. A.; BUIJSSE, B. Habitual chocolate consumption may increase body weight in a dose-response manner. PLoS One, 8, n. 8, p. e70271, 2013.

<https://doi.org/10.1371/journal.pone.0070271>

HÅVERSEN, L.; DANIELSSON, K. N.; FOGELSTRAND, L.; WIKLUND, O. Induction of proinflammatory cytokines by long-chain saturated fatty acids in human macrophages. Atherosclerosis, 202, n. 2, p. 382-393, Feb 2009.

<https://doi.org/10.1016/j.atherosclerosis.2008.05.033>

HEYMSFIELD, S. B.; STANLEY, A.; PIETROBELLI, A.; HEO, M. Simple Skeletal Muscle Mass Estimation Formulas: What We Can Learn From Them. Front Endocrinol (Lausanne), 11, p. 31, 2020.

<https://doi.org/10.3389/fendo.2020.00031>

HIDALGO, M. A.; CARRETTA, M. D.; BURGOS, R. A. Long Chain Fatty Acids as Modulators of Immune Cells Function: Contribution of FFA1 and FFA4 Receptors. Front Physiol, 12, p. 668330, 2021.

<https://doi.org/10.3389/fphys.2021.668330>

HONG, S.; CHANG, Y.; JUNG, H. S.; YUN, K. E. et al. Relative muscle mass and the risk of incident type 2 diabetes: A cohort study. PLoS One, 12, n. 11, p. e0188650, 2017.

<https://doi.org/10.1371/journal.pone.0188650>

HOUSTON, D. K.; NICKLAS, B. J.; DING, J.; HARRIS, T. B. et al. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr, 87, n. 1, p. 150-155, Jan 2008.

<https://doi.org/10.1093/ajcn/87.1.150>

HUANG, S.; RUTKOWSKY, J. M.; SNODGRASS, R. G.; ONO-MOORE, K. D. et al. Saturated fatty acids activate TLR-mediated proinflammatory signaling pathways. J Lipid Res, 53, n. 9, p. 2002-2013, Sep 2012.

<https://doi.org/10.1194/jlr.D029546>

IZQUIERDO, M.; MERCHANT, R. A.; MORLEY, J. E.; ANKER, S. D. et al. International Exercise Recommendations in Older Adults (ICFSR): Expert Consensus Guidelines. J Nutr Health Aging, 25, n. 7, p. 824-853, 2021.

<https://doi.org/10.1007/s12603-021-1665-8>

JANSSEN, I.; HEYMSFIELD, S. B.; WANG, Z. M.; ROSS, R. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. J Appl Physiol (1985), 89, n. 1, p. 81-88, Jul 2000.

<https://doi.org/10.1152/jappl.2000.89.1.81>

KIHARA, A. Very long-chain fatty acids: elongation, physiology and related disorders. J Biochem, 152, n. 5, p. 387-395, Nov 2012.

<https://doi.org/10.1093/jb/mvs105>

KIM, K. M.; JANG, H. C.; LIM, S. Differences among skeletal muscle mass indices derived from height-, weight-, and body mass index-adjusted models in assessing sarcopenia. *Korean J Intern Med*, 31, n. 4, p. 643-650, Jul 2016.

<https://doi.org/10.3904/kjim.2016.015>

KIM, W. J.; SHIN, H. M.; LEE, J. S.; SONG, D. G. et al. Sarcopenia and Back Muscle Degeneration as Risk Factors for Degenerative Adult Spinal Deformity with Sagittal Imbalance and Degenerative Spinal Disease: A Comparative Study. *World Neurosurg*, 148, p. e547-e555, Apr 2021.

<https://doi.org/10.1016/j.wneu.2021.01.053>

KURIYAN, R. Body composition techniques. *Indian J Med Res*, 148, n. 5, p. 648-658, Nov 2018.

https://doi.org/10.4103/ijmr.IJMR_1777_18

LAI, K. Z. H.; YEHA, N. A.; SEMNANI-AZAD, Z.; MEJIA, S. B. et al. Lifestyle Factors Associated with Circulating Very Long-Chain Saturated Fatty Acids in Humans: A Systematic Review of Observational Studies. *Adv Nutr*, 14, n. 1, p. 99-114, Jan 2023.

<https://doi.org/10.1016/j.advnut.2022.10.004>

LEE, D. H.; GIOVANNUCCI, E. L. Body composition and mortality in the general population: A review of epidemiologic studies. *Exp Biol Med (Maywood)*, 243, n. 17-18, p. 1275-1285, Dec 2018.

<https://doi.org/10.1177/1535370218818161>

LEMAITRE, R. N.; FRETTS, A. M.; SITLANI, C. M.; BIGGS, M. L. et al. Plasma phospholipid very-long-chain saturated fatty acids and incident diabetes in older adults: the Cardiovascular Health Study. *Am J Clin Nutr*, 101, n. 5, p. 1047-1054, May 2015.

<https://doi.org/10.3945/ajcn.114.101857>

LEONG, D. P.; TEO, K. K.; RANGARAJAN, S.; LOPEZ-JARAMILLO, P. et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet*, 386, n. 9990, p. 266-273, Jul 18 2015.

[https://doi.org/10.1016/S0140-6736\(14\)62000-6](https://doi.org/10.1016/S0140-6736(14)62000-6)

LI, Z.; LEI, H.; JIANG, H.; FAN, Y. et al. Saturated fatty acid biomarkers and risk of cardiometabolic diseases: A meta-analysis of prospective studies. *Front Nutr*, 9, p. 963471, 2022.

<https://doi.org/10.3389/fnut.2022.963471>

LIPINA, C.; HUNDAL, H. S. Lipid modulation of skeletal muscle mass and function. *J Cachexia Sarcopenia Muscle*, 8, n. 2, p. 190-201, Apr 2017.

<https://doi.org/10.1002/jcsm.12144>

LIU, A. G.; FORD, N. A.; HU, F. B.; ZELMAN, K. M. et al. A healthy approach to dietary fats: understanding the science and taking action to reduce consumer confusion. *Nutr J*, 16, n. 1, p. 53, Aug 30 2017.

<https://doi.org/10.1186/s12937-017-0271-4>

LYNCH, G. S.; KOOPMAN, R. Dietary meat and protection against sarcopenia. *Meat Sci*, 144, p. 180-185, Oct 2018.

<https://doi.org/10.1016/j.meatsci.2018.06.023>

MACDIARMID, J.; BLUNDELL, J. Assessing dietary intake: Who, what and why of under-reporting. *Nutr Res Rev*, 11, n. 2, p. 231-253, Dec 1998.
<https://doi.org/10.1079/NRR19980017>

MANCO, M.; MINGRONE, G.; GRECO, A. V.; CAPRISTO, E. et al. Insulin resistance directly correlates with increased saturated fatty acids in skeletal muscle triglycerides. *Metabolism*, 49, n. 2, p. 220-224, Feb 2000.
[https://doi.org/10.1016/S0026-0495\(00\)91377-5](https://doi.org/10.1016/S0026-0495(00)91377-5)

MITCHELL, C. J.; MILAN, A. M.; MITCHELL, S. M.; ZENG, N. et al. The effects of dietary protein intake on appendicular lean mass and muscle function in elderly men: a 10-wk randomized controlled trial. *Am J Clin Nutr*, 106, n. 6, p. 1375-1383, Dec 2017.
<https://doi.org/10.3945/ajcn.117.160325>

MONTIEL-ROJAS, D.; SANTORO, A.; NILSSON, A.; FRANCESCHI, C. et al. Beneficial Role of Replacing Dietary Saturated Fatty Acids with Polyunsaturated Fatty Acids in the Prevention of Sarcopenia: Findings from the NU-AGE Cohort. *Nutrients*, 12, n. 10, Oct 9 2020.
<https://doi.org/10.3390/nu12103079>

NHANES. Laboratory Procedure Manual. 2011.
<https://doi.org/10.1510/mmcts.2009.004176>

PAPIOL, M.; SERRA-PRAT, M.; VICO, J.; JEREZ, N. et al. Poor Muscle Strength and Low Physical Activity Are the Most Prevalent Frailty Components in Community-Dwelling Older Adults. *J Aging Phys Act*, 24, n. 3, p. 363-368, Jul 2016.
<https://doi.org/10.1123/japa.2015-0114>

PILLON, N. J.; ARANE, K.; BILAN, P. J.; CHIU, T. T. et al. Muscle cells challenged with saturated fatty acids mount an autonomous inflammatory response that activates macrophages. *Cell Commun Signal*, 10, n. 1, p. 30, Oct 19 2012.
<https://doi.org/10.1186/1478-811X-10-30>

PSUTKA, S. P.; BOORJIAN, S. A.; MOYNAGH, M. R.; SCHMIT, G. D. et al. Decreased Skeletal Muscle Mass is Associated with an Increased Risk of Mortality after Radical Nephrectomy for Localized Renal Cell Cancer. *J Urol*, 195, n. 2, p. 270-276, Feb 2016.
<https://doi.org/10.1016/j.juro.2015.08.072>

REID, K. F.; PASHA, E.; DOROS, G.; CLARK, D. J. et al. Longitudinal decline of lower extremity muscle power in healthy and mobility-limited older adults: influence of muscle mass, strength, composition, neuromuscular activation and single fiber contractile properties. *Eur J Appl Physiol*, 114, n. 1, p. 29-39, Jan 2014.
<https://doi.org/10.1007/s00421-013-2728-2>

RODACKI, C. L.; RODACKI, A. L.; PEREIRA, G.; NALIWAIKO, K. et al. Fish-oil supplementation enhances the effects of strength training in elderly women. *Am J Clin Nutr*, 95, n. 2, p. 428-436, Feb 2012.
<https://doi.org/10.3945/ajcn.111.021915>

SANDOVAL-INSAUSTI, H.; PÉREZ-TASIGCHANA, R. F.; LÓPEZ-GARCÍA, E.; GARCÍA-ESQUINAS, E. et al. Macronutrients Intake and Incident Frailty in Older Adults: A Prospective Cohort Study. *J Gerontol A Biol Sci Med Sci*, 71, n. 10, p. 1329-1334, Oct

2016.

<https://doi.org/10.1093/gerona/glw033>

SCHÖNFELD, P.; WOJTCZAK, L. Short- and medium-chain fatty acids in energy metabolism: the cellular perspective. *J Lipid Res*, 57, n. 6, p. 943-954, Jun 2016.

<https://doi.org/10.1194/jlr.R067629>

SCOTT, D.; BLIZZARD, L.; FELL, J.; GILES, G. et al. Associations between dietary nutrient intake and muscle mass and strength in community-dwelling older adults: the Tasmanian Older Adult Cohort Study. *J Am Geriatr Soc*, 58, n. 11, p. 2129-2134, Nov 2010.

<https://doi.org/10.1111/j.1532-5415.2010.03147.x>

SEBE, M.; TSUTSUMI, R.; SENOURA, S.; KISHI, J. et al. Saturated fatty acids intake is associated with muscle atrophy in rheumatoid arthritis. 5, n. 1, p. 86-101, 2022.

<https://doi.org/10.1002/rco2.53>

SEIDEL, D.; BRAYNE, C.; JAGGER, C. Limitations in physical functioning among older people as a predictor of subsequent disability in instrumental activities of daily living. *Age Ageing*, 40, n. 4, p. 463-469, Jul 2011.

<https://doi.org/10.1093/ageing/afr054>

SERGI, G.; DE RUI, M.; VERONESE, N.; BOLZETTA, F. et al. Assessing appendicular skeletal muscle mass with bioelectrical impedance analysis in free-living Caucasian older adults. *Clin Nutr*, 34, n. 4, p. 667-673, Aug 2015.

<https://doi.org/10.1016/j.clnu.2014.07.010>

SERGI, G.; TREVISAN, C.; VERONESE, N.; LUCATO, P. et al. Imaging of sarcopenia. *Eur J Radiol*, 85, n. 8, p. 1519-1524, Aug 2016.

<https://doi.org/10.1016/j.ejrad.2016.04.009>

SHOU, J.; CHEN, P. J.; XIAO, W. H. Mechanism of increased risk of insulin resistance in aging skeletal muscle. *Diabetol Metab Syndr*, 12, p. 14, 2020.

<https://doi.org/10.1186/s13098-020-0523-x>

SMITH, G. I.; JULLIAND, S.; REEDS, D. N.; SINACORE, D. R. et al. Fish oil-derived n-3 PUFA therapy increases muscle mass and function in healthy older adults. *Am J Clin Nutr*, 102, n. 1, p. 115-122, Jul 2015.

<https://doi.org/10.3945/ajcn.114.105833>

SNETSELAAR, L. G.; DE JESUS, J. M.; DESILVA, D. M.; STOODY, E. E. Dietary Guidelines for Americans, 2020-2025: Understanding the Scientific Process, Guidelines, and Key Recommendations. *Nutr Today*, 56, n. 6, p. 287-295, Nov-Dec 2021.

<https://doi.org/10.1097/NT.0000000000000512>

SRIKANTHAN, P.; HORWICH, T. B.; CALFON PRESS, M.; GORNBEIN, J. et al. Sex Differences in the Association of Body Composition and Cardiovascular Mortality. *J Am Heart Assoc*, 10, n. 5, p. e017511, Feb 2021.

<https://doi.org/10.1161/JAHA.120.017511>

STRANDKVIST, V.; LARSSON, A.; PAUELSEN, M.; NYBERG, L. et al. Hand grip strength is strongly associated with lower limb strength but only weakly with postural control in community-dwelling older adults. *Arch Gerontol Geriatr*, 94, p. 104345, May-Jun

2021.

<https://doi.org/10.1016/j.archger.2021.104345>

SZULC, P.; MUNOZ, F.; MARCHAND, F.; CHAPURLAT, R. et al. Rapid loss of appendicular skeletal muscle mass is associated with higher all-cause mortality in older men: the prospective MINOS study. *Am J Clin Nutr*, 91, n. 5, p. 1227-1236, May 2010.

<https://doi.org/10.3945/ajcn.2009.28256>

TATANGELO, T.; MUOLLO, V.; GHIOTTO, L.; SCHENA, F. et al. Exploring the association between handgrip, lower limb muscle strength, and physical function in older adults: A narrative review. *Exp Gerontol*, 167, p. 111902, Oct 1 2022.

<https://doi.org/10.1016/j.exger.2022.111902>

WATERWORTH, S. P.; KERR, C. J.; MCMANUS, C. J.; COSTELLO, R. et al. Obese individuals do not underreport dietary intake to a greater extent than nonobese individuals when data are allometrically-scaled. *Am J Hum Biol*, 34, n. 7, p. e23743, Jul 2022.

<https://doi.org/10.1002/ajhb.23743>

WELCH, A. A.; MACGREGOR, A. J.; MINIHANE, A. M.; SKINNER, J. et al. Dietary fat and fatty acid profile are associated with indices of skeletal muscle mass in women aged 18-79 years. *J Nutr*, 144, n. 3, p. 327-334, Mar 2014.

<https://doi.org/10.3945/jn.113.185256>

WILKINSON, D. J.; PIASECKI, M.; ATHERTON, P. J. The age-related loss of skeletal muscle mass and function: Measurement and physiology of muscle fibre atrophy and muscle fibre loss in humans. *Ageing Res Rev*, 47, p. 123-132, Nov 2018.

<https://doi.org/10.1016/j.arr.2018.07.005>

YU, E.; HU, F. B. Dairy Products, Dairy Fatty Acids, and the Prevention of Cardiometabolic Disease: a Review of Recent Evidence. *Curr Atheroscler Rep*, 20, n. 5, p. 24, Mar 21 2018.

<https://doi.org/10.1007/s11883-018-0724-z>