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

ALINE SILVA DOS REIS

ASSOCIAÇÃO DO CONSUMO DIETÉTICO COM A SARCOPENIA E SEUS COMPONENTES EM INDIVÍDUOS QUE REALIZARAM TRANSPLANTE RENAL

UBERLÂNDIA

2022

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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

</div>

UBERLÂNDIA

2022

UNIVERSIDADE FEDERAL DE UBERLÂNDIA
Coordenação do Programa de Pós-Graduação em Ciências da Saúde
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ATA DE DEFESA - PÓS-GRADUAÇÃO

Programa de Pós-Graduação em:	Ciências da Saúde
Defesa de:	Tese de Doutorado Nº 002/PPCSA
Data:	31.01.2022 Hora de início: 14:00 Hora de encerramento: 18:10
Matrícula do Discente:	11813CSD003
Nome do Discente:	Aline Silva dos Reis
Título do Trabalho:	Associação do Consumo Dietético com a Sarcopenia e seus Componentes em Indivíduos que Realizaram Transplante Renal
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: Profa. Dra. Paula Cândido Nahas (UNA), Profa. Dra. Camila Cremonezi Japur (USP), Profa. Dra. Ana Elisa Madalena Rinaldi (UFU), Profa. Dra. Geórgia das Graças Pena (UFU) e Prof. Dr. Erick Prado de Oliveira (UFU), orientador da candidata.

Iniciando os trabalhos, o presidente da mesa, Prof. Dr. Erick Prado de Oliveira, apresentou a Comissão Examinadora e a candidata, agradeceu a presença do público, e concedeu a Discente a palavra para a exposição do seu trabalho. A duração da apresentação da 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):

<div align="center">Aprovada.</div>

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 **Camila Cremonezi Japur, Usuário Externo**, em

31/01/2022, às 18:12, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do Decreto nº 8.539, de 8 de outubro de 2015.

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FOLHA DE APROVAÇÃO

ALINE SILVA DOS REIS

ASSOCIAÇÃO DO CONSUMO DIETÉTICO COM A SARCOPENIA E SEUS COMPONENTES EM INDIVÍDUOS QUE REALIZARAM TRANSPLANTE RENAL

Presidente da banca: Professor 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.

Banca examinadora

Titular: Professora Dra. Camila Cremonezi Japur

Instituição: Universidade de São Paulo (USP)

Titular: Professora Dra. Paula Cândido Nahas

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Suplente: Professora Dra. Bárbara Perez Vogt

Instituição: Universidade Federal de Uberlândia (UFU)

Suplente: Professora Dra. Luana Padua Soares

Instituição: Universidade Federal de Uberlândia (UFU)

Suplente: Professor Dr. Heitor Bernardes Pereira Delfino

Instituição: Centro Universitário Una-Uberlândia.

DEDICATÓRIA

Aos meus pais, Luiz Antonio e Maria Alice, com todo o meu amor.

AGRADECIMENTOS

"Apenas aqueles que se arriscam a ir longe demais tem a chance de descobrir quão longe podem ir."

(Thomas Stearns Eliot)

RESUMO

Introdução: A perda de massa muscular e de função física (força e capacidade funcional), conhecida como sarcopenia, é prevalente em indivíduos que realizaram transplante renal adultos e idosos. Esta condição clínica está associada ao pior prognóstico e maior risco de morbimortalidade, além de dificultar a execução das atividades de vida diária. Por outro lado, o consumo insuficiente de energia e nutrientes pode contribuir para o desenvolvimento da sarcopenia. Neste sentido, torna-se essencial investigar quais nutrientes podem estar associados à proteção para esta condição clínica nesta população. **Objetivo:** Avaliar a associação entre o consumo dietético e a sarcopenia e seus componentes em indivíduos que realizaram transplante renal. **Material e Métodos:** Foi realizado estudo transversal com indivíduos que realizaram transplante renal acompanhados no ambulatório de transplante renal do Hospital de Clínicas da Universidade Federal de Uberlândia (HC-UFU). A avaliação dietética foi realizada por meio de dois recordatórios alimentares de 24 horas, utilizando o método *five steps multiple-pass*. A avaliação da composição corporal foi realizada por meio da bioimpedância elétrica. A massa muscular esquelética apendicular foi estimada por meio da equação de Sergi et al. (2015). O índice de massa muscular esquelética apendicular foi calculado, o qual consiste na massa muscular esquelética apendicular (kg) dividida pela altura ao quadrado (m²). O teste de força de preensão manual (FPM) e o teste de sentar e levantar da cadeira foram realizados para avaliar a força muscular. A capacidade funcional foi avaliada por meio da bateria curta de desempenho físico (SPPB) e do teste de caminhada de 4 m. A sarcopenia foi diagnosticada por meio do critério proposto pelo Consenso Europeu de Sarcopenia Revisado. Foram realizados diversos modelos estatísticos para verificar a associação entre variáveis dietéticas e a prevalência de sarcopenia, massa muscular, força muscular e capacidade funcional dos participantes. **Resultados:** No primeiro artigo foi demonstrado que a ingestão de ácido graxo ômega-3 foi positivamente associada ao índice de massa muscular esquelética apendicular e a maior ingestão de ácidos graxos poliinsaturados e ômega-3 foi associada a menor chance de apresentar baixo índice de massa muscular esquelética e sarcopenia em toda a amostra. Já no segundo artigo, foi observado que o número de refeições contendo pelo menos 30 gramas de proteína foi negativamente associado ao tempo gasto para realizar o teste de sentar e levantar da cadeira e positivamente associado ao escore do SPPB entre os indivíduos que realizaram transplante renal com 50 anos ou mais, independentemente de fatores de confusão. **Conclusões:** A ingestão de ácido graxo ômega-3 e de ácidos graxos poliinsaturados são fatores de proteção para sarcopenia e baixa massa muscular, mas não para força e capacidade funcional, em indivíduos que realizaram transplante renal. Adicionalmente, o número de refeições contendo pelo menos 30 gramas de proteína está associado a um melhor desempenho no teste de sentar e levantar da cadeira e no SPPB em pacientes indivíduos que realizaram transplante renal com 50 anos ou mais. Ensaios clínicos randomizados futuros devem ser realizados para avaliar o efeito destes nutrientes sobre a sarcopenia e seus componentes em indivíduos que realizaram transplante renal.

Palavras-Chave: Consumo Alimentar; Desempenho Físico Funcional; Doença Renal Cônica; Força Muscular; Músculo Esquelético; Sarcopenia; Transplante Renal.

ABSTRACT

Introduction: The loss of muscle mass and physical function (strength and functional capacity), known as sarcopenia, is prevalent in adult and older adults kidney transplant patients. This clinical condition is associated with a worse prognosis and greater risk of morbidity and mortality, in addition to making it difficult to carry out activities of daily living. On the other hand, insufficient consumption of energy and nutrients can contribute to the development of sarcopenia. In this sense, it is essential to investigate which nutrients may be associated with protection for this clinical condition in this population. **Aim:** To evaluate the association between dietary intake and sarcopenia and its components in kidney transplant patients. **Material and Methods:** A cross-sectional study was performed at a clinical hospital of the Federal University of Uberlandia, Minas Gerais, Brazil; evaluating kidney transplant patients (KTPs) at the kidney transplantation ambulatory clinic. Dietary assessment was performed using two 24-hour dietary recalls, using the five steps multiple-pass method. The assessment of body composition was performed using bioimpedance. Appendicular skeletal muscle mass was estimated using the equation by Sergi et al. (2015). The appendicular skeletal muscle mass index was calculated, which consists of the appendicular skeletal muscle mass (kg) divided by the height squared (m²). The handgrip strength test (HGS) and five times sit to stand test (5STS) were performed to assess muscle strength. Functional capacity was assessed using the short physical performance battery (SPPB) and the 4-m walking test. Sarcopenia was diagnosed using the criteria proposed by the Revised European Consensus on Sarcopenia. Several statistical models were performed to verify the association between dietary variables and prevalence of sarcopenia, muscle mass, muscle strength and functional capacity of the participants. **Results:** In the first article, it was shown that omega-3 fatty acid intake was positively associated with appendicular skeletal muscle mass index and higher intake of polyunsaturated and omega-3 fatty acids was associated with a lower chance of having low muscle mass index skeletal and sarcopenia in total sample. In the second article, it was observed that the number of meals containing at least 30 grams of protein was negatively associated with the time to perform 5STS and positively associated with the SPPB score among KTPs aged 50 years or more, regardless of confounding factors. **Conclusions:** Intake of omega-3 fatty acids and polyunsaturated fatty acids are protective factors for sarcopenia and low muscle mass, but not for strength and functional capacity, in KTPS. Additionally, the number of meals containing at least 30 grams of protein is associated with better performance on 5STS and SPPB in KTPs aged 50 years and over. Future randomized controlled trials should be performed to assess the effect of these nutrients on sarcopenia and its components in KTPs.

Keywords: Chronic Kidney Disease; Food consumption; Kidney transplantation; Muscle Strength; Skeletal muscle; Sarcopenia; Physical Functional Performance.

LISTA DE ILUSTRAÇÕES

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Artigo 1: Intake of polyunsaturated fatty acids and ω-3 are protective factors for sarcopenia in kidney transplant patients.

Artigo 2: Association of the number of meals containing at least 20 and 30 grams of protein with muscle mass, strength and functional capacity in kidney transplant patients.

LISTA DE ABREVIATURAS E SIGLAS

FUNDAMENTAÇÃO TEÓRICA

ABTO	Associação Brasileira de Transplante de Órgãos
COVID-19	Novo Coronavírus
DEXA	Absormetria de Raios-X de Dupla Energia
DRC	Doença Renal Crônica
EUA	Estados Unidos da América
SPPB	*Short Physical Performance Battery*
TFG	Taxa de Filtração Glomerular
TRS	Terapia Renal Substitutiva
TUG	*Timed-Up-and-Go Test*

ARTIGOS

5STS	*Five Times Sit to Stand Test*
ANOVA	*One-way Analysis of Variance*
ASMI	*Appendicular Skeletal Muscle Mass Index*
ASMM	*Appendicular Skeletal Muscle Mass*
BCAA	Branched Chain Amino Acids
BMI	*Body mass index*
CKD	*Chronic Kidney Disease*
CKD-EPI	*Chronic Kidney Disease Epidemiology Collaboration Equation*
CRP	*C-Reactive Protein*
CV	Coefficient of Variation
GFR	*Glomerular Filtration Rate*

HGS	*Handgrip Strength*
IPAQ	*International Physical Activity Questionnaire*
KTPs	*Kidney Transplant Patients*
MUFAs	*Monounsaturated Fatty Acids*
NDSR	*Nutrition Data System for Research*
PAL	*Physical Activity Level*
PhAº	*Phase Angle*
PUFAs	*Polyunsaturated Fatty Acids*
SD	*Standard Deviation*
SFAs	*Saturated Fatty Acids*
SPPB	*Short Physical Performance Battery*
ω-3	*Omega 3*
ω-6	*Omega 6*
WC	*Waist Circumference*
χ^2	*Chi-squared*

SUMÁRIO

1 INTRODUÇÃO

O termo sarcopenia tem origem grega, em que "*sarx*" corresponde à músculo e "*penia*" à perda, portanto, sarcopenia significa perda de músculo (ROSENBERG, 1989). No passado, a sarcopenia era definida como a depleção muscular que ocorre no envelhecimento (BAUMGARTNER *et al*., 1998). Posteriormente, os componentes de força muscular e capacidade funcional foram incorporados ao conceito (CRUZ-JENTOFT *et al*., 2010). E mais recentemente, o Consenso Europeu de Sarcopenia Revisado propôs que a força deveria ser o principal componente para o diagnóstico da mesma (CRUZ-JENTOFT *et al*., 2019). Sendo assim, considera-se como sarcopênico, o indivíduo que possui força muscular diminuída e concomitantemente massa muscular reduzida. Quando o indivíduo apresenta baixa força e baixa massa muscular e ao mesmo tempo, prejuízo de sua capacidade funcional, é considerado como sarcopênico grave (CRUZ-JENTOFT *et al*., 2019).

Em um estudo prévio de nosso grupo de pesquisa, foi demonstrado que aproximadamente 19% dos indivíduos que realizaram transplante renal avaliados apresentavam sarcopenia (LIMIRIO *et al*., 2020). Existem várias causas que podem provocar sarcopenia em indivíduos que realizaram o transplante renal, além do envelhecimento. Indivíduos que realizaram transplante renal apresentam características que os diferenciam da população em geral, como o uso de imunossupressores e corticosteroides por toda a vida para reduzir o risco de rejeição do enxerto (SABATINO *et al*., 2021). O uso desses fármacos, por sua vez, interfere na massa muscular e pode afetar a força muscular e a capacidade funcional (SATO *et al*., 2017; CATIć-ĐORđEVIć *et al*., 2017). Adicionalmente, esses indivíduos conviveram com a doença renal crônica (DRC) por anos. Na fase de tratamento conservador, esses pacientes sofreram restrição no consumo de proteínas para retardar a perda da função renal residual. Na fase dialítica, esses pacientes comumente reduzem a prática de atividade física, tornam-se sedentários e perdem nutrientes no dialisato (SOUZA *et al*., 2015; SABATINO *et al*., 2021). Outras características da DRC são uremia, aumento do estresse oxidativo e inflamação (WATANABE, ENOKI, MARUYAMA, 2019). Assim, indivíduos submetidos ao transplante renal podem ter perdido massa muscular, força, desempenho físico e capacidade funcional antes do transplante, e esses prejuízos podem se intensificar com o uso contínuo de imunossupressores e corticosteroides no período pós-

transplante (GIL *et al*.,2020). Por todas essas razões, os indivíduos que realizaram transplante renal são considerados um grupo de risco para depleção muscular, redução da força muscular e do desempenho físico/capacidade funcional e desenvolvimento de sarcopenia.

No melhor de nosso conhecimento, estudos avaliando a associação entre a ingestão alimentar (uma das causas da sarcopenia) e a sarcopenia e seus componentes em indivíduos que realizaram transplante renal não foram encontrados até a publicação do primeiro artigo da presente tese, o que configura uma importante lacuna de conhecimento na literatura. Alguns estudos têm associado o consumo alimentar com sarcopenia em idosos sem doença renal e foi observado que maior ingestão de frutas, vegetais (KIM *et al*., 2015), proteínas (HUANG *et al*., 2016) e ácidos graxos ômega-3 (TER BORG *et al*., 2016) são possíveis fatores de proteção nutricional para sarcopenia. Outros estudos realizados com idosos avaliaram a associação da distribuição de proteínas ao longo do dia e/ou a adequação da dose de proteína por refeição com a massa magra (DE BRANCO *et al*, 2021; LOENNEKE *et al*.,2016; HAYASHI *et al*., 2020), massa muscular (HAYASHI et al., 2020), força muscular e capacidade funcional (GINGRICH *et al*., 2017), com resultados conflitantes. Alguns desses estudos encontraram associações positivas (DE BRANCO *et al*, 2021; LOENNEKE *et al*.,2016; HAYASHI *et al*., 2020), enquanto outro não (GINGRICH *et al*., 2017).

Considerando que os indivíduos que realizaram transplante renal apresentam causas adicionais para o desenvolvimento da sarcopenia e para a alteração de seus componentes (força muscular, massa muscular e capacidade funcional) em comparação com outras populações, como mencionado acima, ainda é desconhecido quais elementos da dieta estão associados à sarcopenia e aos seus componentes nesta população. Portanto, o objetivo da presente tese foi associar a ingestão alimentar com a sarcopenia e seus componentes nos indivíduos que realizaram transplante renal.

1.1 Considerações Iniciais

A formatação da presente tese de doutorado foi elaborada de acordo com o modelo alternativo sugerido pelo Programa de Pós-graduação em Ciências da Saúde, da Faculdade de Medicina, Universidade Federal de Uberlândia, o qual estabelece que os resultados do estudo sejam demonstrados no formato de artigos científicos.

A Tese está organizada nas seguintes seções: **Fundamentação Teórica**, em que se apresenta a revisão da literatura sobre os temas abordados na tese; **Objetivos**, em que os propósitos do estudo são evidenciados; **Resultados**, que consiste nos dois manuscritos elaborados; **Conclusão**, que discorre sobre um apanhado geral dos principais resultados do estudo; **Perspectivas,** em que são apresentadas as expectativas para estudos futuros; **Pós-texto,** que inclui referências bibliográficas, anexos e apêndices.

O primeiro manuscrito intitulado **"*Intake of polyunsaturated fatty acids and ω-3 are protective factors for sarcopenia in kidney transplant patients*"** teve como objetivo associar o consumo alimentar de carboidratos, proteínas totais, proteína animal, proteína vegetal, proteína em gramas por kg de peso, gorduras totais, gorduras saturadas, gorduras monoinsaturadas, gorduras poliinsaturadas, ácido graxo ômega-6 e ácido graxo ômega-3 com a sarcopenia e seus componentes em indivíduos que realizaram transplante renal . Esse artigo teve sua versão final publicada em janeiro de 2021 na revista *Nutrition* (*Impact Factor* = 4.008).

O segundo manuscrito intitulado **"*Association of the number of meals containing at least 20 and 30 grams of protein with muscle mass, strength and functional capacity in kidney transplant patients*"**, teve como objetivo associar o número de refeições contendo pelo menos 20 e 30 gramas de proteína com a massa muscular, força muscular e a capacidade funcional em indivíduos que realizaram transplante renal e pretende-se submetê-lo à revista *European Journal of Clinical Nutrition* (*Impact Factor* = 4.016).

2 FUNDAMENTAÇÃO TEÓRICA

2.1 Doença Renal Crônica e Transplante Renal

Entende-se como doença renal crônica (DRC) a perda progressiva e irreversível da função renal. No estágio terminal da DRC, os rins tornam-se incapazes de manter o equilíbrio metabólico e hidroeletrolítico do indivíduo. A gravidade da DRC é estratificada em cinco estágios segundo a Taxa de Filtração Glomerular (TFG). No primeiro estágio da DRC há dano renal (proteinúria), porém com TFG preservada (> 90 mL/min/1,73m²). No segundo estágio da DRC, além do dano renal o indivíduo já passa a apresentar discreta redução da TFG (60 a 80 mL/min/1,73m²). No terceiro estágio da DRC ocorre redução moderada da TFG (30 a 59 mL/min/1,73m²). No quarto estágio da DRC ocorre diminuição significativa e grave da TFG (15 a 30 mL/min/1,73m²). Já no quinto e último estágio da DRC ocorre a falência renal com TFG inferior a 15 mL/min/1,73m². Pacientes com DRC em estágio terminal precisam utilizar métodos de filtração artificial do sangue, como hemodiálise ou diálise peritoneal, também denominadas de Terapia Renal Substitutiva (TRS) ou realizar transplante renal, para garantir a sua sobrevivência (NATIONAL KIDNEY FOUNDATION, 2002).

Transplante é definido como o procedimento cirúrgico que transfere órgão ou tecido de um indivíduo para outro visando substituir ou compensar a função perdida. No transplante renal, implanta-se um rim saudável em um paciente portador de DRC em estágio terminal (ABTO, 2012). Segundo o Registro Brasileiro de Transplantes, o Brasil é o segundo país em número absoluto em realização de transplantes renais, ficando atrás somente dos Estados Unidos da América (EUA). O número de transplantes renais vinha crescendo em curva ascendente no país desde 2016 até 2019 com ligeira queda em 2020 devido a emergência em saúde pública ocasionada pela pandemia do novo Coronavírus (COVID-19) que chegou ao Brasil em meados de março do referido ano. No ano de 2020, foram realizados 4805 transplantes de rim no país, o que equivale a 1478 transplantes a menos em relação ao ano anterior. O estado de Minas Gerais foi o segundo em número absoluto de realização de transplantes renais no período, com 526 procedimentos realizados, perdendo apenas para o estado de São Paulo, o qual realizou 1770 transplantes renais no mesmo ano (ABTO, 2020). Apesar da diminuição da frequência de transplantes no país desde o início da pandemia do novo Coronavírus, o Brasil continuou apresentando número

elevado de transplantes renais, sendo que de janeiro a setembro de 2021 haviam sido realizados 3304 transplantes de rim no país, e destes, 389 ocorreram no estado de Minas Gerais (ABTO, 2021).

O transplante renal é considerado o melhor tratamento para indivíduos com DRC em estágio terminal, mas para minimizar o risco de rejeição, após o transplante é necessário o uso de medicamentos imunossupressores por toda a vida. Um estudo recente mostrou que a qualidade de vida e a força muscular dos pacientes após seis meses do transplante renal melhoraram em relação ao período pré-transplante, independentemente das altas doses dos imunossupressores utilizados. Porém, apesar dessa melhora, os participantes permaneceram com força muscular e qualidade de vida insatisfatórias (GIL *et al*., 2020).

2.2 Sarcopenia e Doença Renal Crônica

2.2.1 Contexto Histórico e Evolução das Definições e Critérios de Diagnóstico de Sarcopenia

No ano de 1931, o neurologista britânico Macdonald Critchley, foi o primeiro na literatura científica moderna a conectar a perda de músculo esquelético ao envelhecimento ao observar que a musculatura tende a diminuir nos idosos (CRITCHLEY, 1931). Em 1989, o pesquisador Irwin H. Rosenberg foi pioneiro ao lançar a discussão sobre a perda de massa magra que ocorre com o envelhecimento em um congresso de geriatria. Dessa forma, ele sugeriu que para que maior atenção fosse dada a este problema seria necessário dar a ele um nome e propôs os termos sarcopenia e sarcomalácia para descrever tal fenômeno, sendo que sarcopenia foi o termo adotado (ROSENBERG, 1989). Os primeiros pontos de corte para sarcopenia em cada sexo foram definidos como valores abaixo de 2 desvios-padrão da massa muscular apendicular média da população referência do estudo Rosetta (BAUMGARTNER *et al*., 1998).

Estudos científicos sobre sarcopenia começaram a ser publicados a partir dos anos 90 e o número de artigos cresceu ainda mais a partir dos anos 2000 (MORLEY; ANKER; VON HAEHLING, 2014). Com base nestes trabalhos, em 2010 foi publicado o Consenso Europeu de Sarcopenia, que inovou ao incorporar os componentes funcionais de força muscular e capacidade funcional ao critério de diagnóstico da sarcopenia (CRUZ-JENTOFT *et al*., 2010). De acordo com este Consenso, a sarcopenia foi definida como uma síndrome geriátrica caracterizada por perda

progressiva e generalizada de massa muscular esquelética e força com risco de desfechos desfavoráveis. O Consenso recomendou então, o uso da presença de massa muscular baixa e baixa função muscular (força ou desempenho) para o diagnóstico de sarcopenia. Assim, o diagnóstico exigia a identificação de baixa massa muscular, mais a detecção de qualquer prejuízo de força muscular ou desempenho físico em testes de capacidade funcional. Ainda de acordo com este Consenso, a massa muscular poderia ser avaliada por meio de absormetria de raios-x de dupla energia (DEXA) ou bioimpedância elétrica com uso de equações preditivas, a força muscular por meio do teste de força de preensão manual e o desempenho físico por meio do teste de caminhada de 4 metros ou pelo *short physical performance battery* (SPPB) (CRUZ-JENTOFT *et al*., 2010).

A definição e o critério de diagnóstico publicados em 2010 no Consenso Europeu de Sarcopenia promoveram avanços na identificação e atendimento de pessoas em risco ou com sarcopenia, adicionalmente, pesquisadores de todo o mundo avançaram notavelmente na compreensão do músculo e seus papéis na saúde e na doença e muitos estudos sobre sarcopenia foram publicados desde então. Muitos desses estudos demonstraram que a perda de força muscular estava associada a piores desfechos do que a baixa massa muscular e por este motivo, na atualização do consenso publicada em 2019, a força muscular passou a ser o primeiro e principal componente para o diagnóstico da sarcopenia. Dessa maneira, a sarcopenia foi definida como uma doença muscular (falência muscular) ocasionada por alterações musculares adversas que se acumulam ao longo da vida; sendo comum entre adultos mais velhos, mas que também pode ocorrer mais cedo na vida adulta e passou a ser diagnosticada pela presença de baixa força muscular concomitantemente à baixa massa muscular e considerada grave quando em associação com a baixa capacidade funcional. O Consenso Europeu de Sarcopenia revisado também inovou ao ampliar a gama de metodologias para a avaliação da massa muscular, força e capacidade funcional. Sendo assim, passaram a ser válidos para a avaliação da força muscular o teste de força de preensão manual e o teste de sentar e levantar da cadeira (considerado um *proxy* da força dos membros inferiores). Para a avaliação da quantidade e qualidade da massa muscular incluíram o DEXA, bioimpedância elétrica e métodos de imagem como tomografia computadorizada e ressonância magnética. Já para a aferição da capacidade funcional foram propostos os testes de velocidade

de marcha, teste de caminhada de 400 m, SPPB e *timed-up-and-go test* (TUG) (CRUZ-JENTOFT *et al*., 2019). Estudos têm demonstrado que há baixa concordância entre a prevalência de sarcopenia avaliada por meio dos critérios de 2010 e de 2019 dos Consensos de Sarcopenia (LIMIRIO *et al*., 2020, VILLANI et al., 2020, OLIVEIRA *et al*., 2021). Recente estudo de revisão sistemática concluiu que o Consenso Europeu de Sarcopenia Revisado parece ser pior que o Consenso original para a predição de desfechos desfavoráveis, porém, com base em evidências limitadas (FERNANDES *et al*., 2021). Novos estudos que avaliem qual deles é melhor em predizer desfechos negativos em saúde e mortalidade são necessários para identificar qual é o mais apropriado para ser utilizado em pesquisas como também na prática clínica.

2.2.2 Distinguindo os Conceitos: Desnutrição, Caquexia e Sarcopenia

A desnutrição/desnutrição proteico-energética, caquexia e sarcopenia são achados comuns em indivíduos com DRC. Pacientes renais crônicos, em geral, podem apresentar inflamação, aumento do catabolismo proteico, ingestão insuficiente de energia e nutrientes, envelhecimento, presença de outras comorbidades, redução do apetite, estilo de vida sedentário, perda de nutrientes no dialisato e resistência à ação dos hormônios anabólicos. Todas essas características podem favorecer ao desenvolvimento das três condições clínicas citadas - desnutrição, caquexia e sarcopenia. Estas três síndromes, por sua vez, podem resultar em baixa qualidade de vida, aumento do risco de quedas e fraturas e aumento das taxas de hospitalização e mortalidade. Tais condições possuem fatores etiológicos e desfechos clínicos comuns, no entanto, embora haja sobreposições entre esses conceitos, os mesmos não são sinônimos (SABATINO *et al*., 2021).

A desnutrição é a perda de peso corporal e gordura corporal devido à ingestão insuficiente de energia e de nutrientes, enquanto que a desnutrição proteico-energética tem um critério similar, mas com um baixo de grau de inflamação como uma condição etiológica adicional (FOUQUE *et al*., 2008). A sarcopenia, por outro lado, é entendida como perda concomitante de força muscular e músculo que ocorre com o envelhecimento, mas que também pode ocorrer mais cedo na vida adulta (CRUZ-JENTOFT *et al*., 2019). Já a caquexia é uma síndrome presente em doenças com inflamação crônica e aumento da degradação de proteínas musculares, e é caracterizada por perda muscular grave que pode ou não ser acompanhada de perda de gordura (CRUZ-JENTOFT *et al*., 2010). Sendo assim, um sujeito com desnutrição

também pode ter sarcopenia, mas não necessariamente ter caquexia, enquanto que um indivíduo com caquexia pode apresentar desnutrição e sarcopenia (SABATINO *et al*., 2021).

2.2.3 Diferenças entre a Sarcopenia Primária e a Sarcopenia Relacionada à Doença Renal Crônica

A sarcopenia primária é relacionada com o envelhecimento, sem outras causas evidentes. A mesma ocorre em decorrência de processos inerentes ao envelhecimento, como a redução das concentrações de hormônios anabólicos, redução do fluxo sanguíneo muscular, número de células satélites e unidades motoras, apoptose celular, disfunção mitocondrial, desuso por imobilização e/ou inatividade física, caquexia, entre outros. Já a sarcopenia secundária pode ser provocada por condições relacionadas à baixa atividade física, como a restrição ao leito, sedentarismo, condições de descondicionamento físico; relacionada à falência orgânica avançada (como é o caso da DRC) e relacionada à nutrição, resultando de ingestão inadequada de energia e/ou proteína, bem como má absorção, distúrbios gastrintestinais ou uso de medicamento que provocam anorexia (CRUZ-JENTOFT *et al*., 2010).

Diversos fatores etiológicos podem ocasionar a perda de massa muscular na DRC. Os mesmos podem estar relacionados a várias condições, incluindo a própria doença renal, o tratamento dialítico e à inflamação crônica. Em conjunto, estes elementos aumentam a degradação e diminuem a síntese de proteínas, levando a um balanço proteico negativo. Dentre os fatores que reduzem a síntese proteica, destacam-se a redução do apetite e restrições alimentares, o envelhecimento, o sedentarismo, a redução do estímulo para regeneração muscular, a redução da atividade física e da ingestão de energia e proteína nos dias de diálise, além da perda de aminoácidos no dialisato. Já dentre os fatores que podem aumentar a degradação de proteínas incluem-se a inflamação, a deficiência de vitamina D, a disbiose intestinal, a incompatibilidade da membrana da diálise, a obesidade, a resistência à insulina, a acidose metabólica e o estresse oxidativo. Tendo em vista que os pacientes renais estão em processo de envelhecimento, não se deve esquecer que o avanço da idade é também uma causa importante de sarcopenia na DRC. Neste sentido, é possível que os pacientes renais crônicos mais velhos sejam mais vulneráveis às alterações musculares durante o processo de envelhecimento do que seus pares sem

DRC, e também em comparação com a população com DRC mais jovem. Portanto, além das causas adicionais, o envelhecimento *per si*, também é um fator que contribui para a etiologia da sarcopenia na DRC (SABATINO *et al.*, 2021).

Comparando a sarcopenia relacionada à DRC e a sarcopenia relacionada ao envelhecimento em termos de metabolismo proteico e energético, mudanças da gordura corporal e alteração de fibras musculares, resistência à insulina e a inflamação, podemos observar que na sarcopenia relacionada à DRC a degradação proteica muscular está aumentada, enquanto que na sarcopenia primária, fica inalterada. Já a síntese proteica muscular se encontra diminuída tanto na sarcopenia relacionada à DRC quanto na relacionada ao envelhecimento. Com relação ao gasto energético de repouso, o mesmo pode se manter normal ou ficar aumentado na sarcopenia relacionada à DRC, enquanto que na sarcopenia relacionada ao envelhecimento se mantém normal. A gordura corporal pode permanecer inalterada, estar aumentada ou diminuída na sarcopenia relacionada à DRC, porém, na sarcopenia primária, normalmente fica aumentada. No que diz respeito às alterações das fibras musculares, é comum que ocorra atrofia das fibras do tipo I e II na sarcopenia relacionada à DRC, enquanto que na sarcopenia primária, ocorre principalmente perda das fibras musculares do tipo II. A inflamação geralmente está aumentada na sarcopenia relacionada à DRC e pode ficar normal ou aumentada na sarcopenia relacionada ao envelhecimento, já a resistência à insulina, geralmente está presente tanto na sarcopenia relacionada à DRC, quanto na sarcopenia primária (SABATINO *et al.*, 2021).

Atualmente, não se tem conhecimento de critérios de diagnóstico de sarcopenia específicos para indivíduos com DRC e/ou indivíduos que realizaram transplante renal. Dessa forma, tem-se admitido a aplicação dos critérios de diagnóstico de sarcopenia próprios para os idosos, também nestas populações (SABATINO *et al.*, 2021). O mesmo se observa no que se refere às equações preditivas para estimar a massa muscular apendicular por meio do exame de bioimpedância elétrica (CARRERO, *et al.*,2016). Em virtude da inexistência de equações preditivas da massa muscular esquelética apendicular em pacientes renais/transplantados até o presente momento, a equação de Sergi *et al.* (2015) que é sugerida pelo consenso europeu de sarcopenia também tem sido utilizada para estimar a massa muscular dos pacientes renais (SERGI *et al.*, 2015, CARRERO *et al.*, 2016, CRUZ-JENTOFT *et al.*, 2019).

Ressalta-se que ainda não foram descritos pontos de corte específicos para a população com DRC para os componentes de força muscular, massa muscular e capacidade funcional e por este motivo deve-se ter cautela ao utilizar estes parâmetros para classificar os pacientes renais (SABATINO *et al.*, 2021). Devido às diferenças observadas nos fatores etiológicos da sarcopenia relacionada à DRC (sarcopenia urêmica) e da sarcopenia relacionada ao envelhecimento (sarcopenia primária), é desejável que no futuro sejam desenvolvidas equações preditivas para massa muscular, pontos de corte específicos para os componentes da sarcopenia, bem como um critério de diagnóstico próprio para pacientes com DRC.

2.3 Consumo Alimentar e Sarcopenia no Pós-Transplante Renal

Alguns estudos têm avaliado a associação entre a dieta e a sarcopenia em idosos, sendo que alguns padrões dietéticos são protetores e outros aumentam a chance de ter sarcopenia. Em um estudo populacional realizado com idosos com 65 anos ou mais na Coréia com 823 homens e 1089 mulheres verificou que a frequência de ingestão de frutas e vegetais foi associada à menor chance de ter sarcopenia após controle por covariáveis em homens. Os homens que estavam no maior quintil de consumo de frutas e vegetais apresentaram menor chance de sarcopenia enquanto que as mulheres com alto consumo apresentaram menor chance de ter sarcopenia (KIM *et al.*, 2015). O maior consumo de proteína total e proteína vegetal foi associado com menor chance de apresentar baixa massa muscular e foi protetor para o status de pré-sarcopenia em um estudo com 327 idosos da comunidade (HUANG *et al.*,2016).

Em alguns estudos o consumo alimentar foi classificado de acordo com determinados padrões alimentares e posteriormente associados com a sarcopenia. Foi observado que o padrão alimentar britânico tradicional foi associado com risco aumentado para sarcopenia em idosos com 85 anos ou mais, mesmo com o consumo proteico total diário adequado (≥ 1.0 g/ kg/dia) (GRANIC *et al.*, 2020). Por outro lado, o consumo de dietas com o padrão alimentar similar à dieta do Mediterrâneo foi protetor para a sarcopenia em alguns estudos. No estudo desenvolvido por Hashemi e colaboradores (2015) foi observado que os idosos do maior tercil do padrão dietético Mediterrâneo tiveram menor chance de apresentar sarcopenia em relação aos do menor tercil (HASHEMI *et al.*,2015). Já a pesquisa conduzida por Karlsson *et al.* (2019) avaliou se o hábito alimentar aos 71 anos influenciou no status de sarcopenia

16 anos mais tarde. Foi demonstrado que o aumento do escore da dieta do Mediterrâneo foi inversamente associado à sarcopenia (KARLSOON *et al*.,2019). Em um estudo realizado com mulheres idosas, foi verificado que as mulheres nos quartis superiores dos padrões alimentares Mediterrâneo e do Mar Báltico apresentaram menor perda de massa magra em 3 anos e no momento inicial maior massa magra, velocidade de caminhada, escore do SPPB e qualidade muscular. Dessa forma, os autores concluíram que a maior aderência aos padrões alimentares do Báltico e do Mediterrâneo pode reduzir o risco para sarcopenia em mulheres idosas (ISANEJAD *et al*., 2017).

Outros estudos realizados com idosos avaliaram a associação da distribuição de proteínas ao longo do dia e/ou a adequação da dose de proteína por refeição com a massa magra (DE BRANCO *et al*, 2021; LOENNEKE *et al*.,2016; HAYASHI *et al*., 2020), massa muscular (HAYASHI et al., 2020), força muscular e capacidade funcional (GINGRICH *et al*., 2017), com resultados conflitantes. Alguns desses estudos encontraram associações positivas (DE BRANCO *et al*, 2021; LOENNEKE *et al*.,2016; HAYASHI *et al*., 2020), enquanto outro não (GINGRICH *et al*., 2017).

Diante do exposto é possível concluir que a relação entre o consumo alimentar e a sarcopenia e seus componentes ainda não está totalmente esclarecida em adultos mais velhos. Levando em conta que as causas da sarcopenia em pacientes que realizaram transplante renal diferem daquelas relacionadas ao envelhecimento, estudos que avaliem a associação entre o consumo alimentar e a sarcopenia e seus componentes nessa população são necessários. Adicionalmente, no melhor de nosso conhecimento, até a publicação do primeiro artigo da presente tese, não havia nenhum outro estudo que avaliasse a associação entre o consumo alimentar e a sarcopenia em indivíduos que realizaram transplante renal, o que justificou a execução do presente trabalho. Portanto, o objetivo da presente tese foi foi associar a ingestão alimentar com a sarcopenia e seus componentes nos indivíduos que realizaram transplante renal. Com a realização deste trabalho, espera-se encontrar associações entre os nutrientes da dieta e sua forma de consumo com a sarcopenia e seus componentes. Dessa forma, será possível gerar evidências transversais para a realização de novos estudos de intervenção dietética para indivíduos que realizaram transplante renal e assim futuramente impactar em novas recomendações nutricionais para este público com a finalidade de prevenir e/ou tratar a sarcopenia.

3 OBJETIVOS

3.1 Objetivo Geral

Avaliar a associação do consumo dietético com a sarcopenia e seus componentes (força muscular, massa muscular e desempenho físico em testes de capacidade funcional) em indivíduos que realizaram transplante renal.

3.2 Objetivos Específicos

- Associar o consumo alimentar de carboidratos, proteínas totais, proteína animal, proteína vegetal, proteína em gramas por kg de peso, gorduras totais, gorduras saturadas, gorduras monoinsaturadas, gorduras poliinsaturadas, ácido graxo ômega-6 e ácido graxo ômega-3 com a sarcopenia e seus componentes em indivíduos que realizaram transplante renal (Artigo 1).

- Associar o número de refeições contendo pelo menos 20 e 30 gramas de proteína com a massa muscular, força muscular e a capacidade funcional em diferentes testes físicos em indivíduos que realizaram transplante renal (Artigo 2).

4 RESULTADOS

Artigo 1: Artigo intitulado "*Intake of polyunsaturated fatty acids and ω-3 are protective factors for sarcopenia in kidney transplant patients*", publicado na revista Nutrition (*Impact Factor* = 4.008): Nutrition. 2021 Jan; 81: 110929. doi: 10.1016/j.nut.2020.110929. Epub 2020 Jul 3.

Intake of polyunsaturated fatty acids and ω-3 are protective factors for sarcopenia in kidney transplant patients

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Abstract

Objectives: The aim of this study was to associate dietary intake with sarcopenia and its components in kidney transplant patients (KTPs).

Methods: A cross-sectional study was performed with 125 KTPs. Strength was evaluated by handgrip strength (HGS) and appendicular muscle mass was estimated by bioelectrical impedance. Functional capacity was assessed by 4-m walking test. Sarcopenia was diagnosed by revised European Consensus on Definition and Diagnosis (2019). Dietary assessment was carried out through two 24-h dietary recalls. It evaluated the consumption of energy (kcal), carbohydrates, protein (total and from animal and vegetable food sources), total fat, saturated fatty acids, monounsaturated fatty acids (MUFAs), polyunsaturated fatty acids (PUFAs), and ω-3 (g) and ω -6 (g).

Results: Intake of ω-3 was positively associated with appendicular skeletal muscle mass index (ASMI; kg/m2). The greater intake of PUFA (g and %) and ω-3 (g) was associated with lower chance to present low ASMI and sarcopenia. None of the other dietary components evaluated in the present study were associated with ASMI and sarcopenia. Walking speed and HGS were not associated with dietary variables.

Conclusions: Intake of ω-3 and PUFAs are protective factors for sarcopenia and low muscle mass, but not for strength and functional capacity, in KTPs.

Keywords: Food consumption; Kidney transplantation; ω-3; Skeletal muscle; Sarcopenia.

Introduction

Sarcopenia is defined as loss of strength, decreased muscle mass,and low functional capacity [1]. We recently showed that ~19% of kidney transplant patients (KTPs) attended in an outpatient clinic presented with sarcopenia [2], which can be an important health problem as patients with chronic kidney disease and sarcopenia may have poor quality of life [3] and increased risk for mortality [4].

There are several causes for sarcopenia in KTPs, such as uremia, medicine use (with proteolytic action [5]), metabolic acidosis, loss of nutrients in dialysis [68],

increased inflammation and oxidative stress [9], aging, hormonal changes, low physical activity levels [7,10], and inadequate dietary intake [11].

To the best of our knowledge, there are no studies evaluating the association between dietary intake (one of the causes of sarcopenia) and sarcopenia and its components in KTPs, which is na important knowledge gap in the literature. Several studies have associated dietary intake with sarcopenia in older adults without kidney disease [1217] and it has been observed that greater intake of fruits, vegetables [12], protein [13] and ω-3 fatty acids [18] are possible nutritional protective factors for sarcopenia. However, considering that KTPs present with additional causes for sarcopenia compared with other populations (such as increased inflammation, oxidative stress, and uremic toxins [19]), it is unknown which dietary components are associated with sarcopenia in this clinical population. Therefore, we aimed to associate dietary intake with sarcopenia and its components in KTPs.

Methods

Study design and participants

A cross-sectional study was performed at a clinical hospital of the Federal University of Uberlandia, Minas Gerais, Brazil; evaluating KTPs at the kidney transplantation ambulatory clinic. Age 18 y and minimum of 3 mo of kidney transplantation were the inclusion criteria. Participants who were unable to answer the questions or to perform the sarcopenia evaluation; KTPs on dialysis, with kidney graft rejection, failure, or both; and participants who did not respond to dietary intake recalls were excluded from the study. In all, 360 patients were attended at the kidney transplantation ambulatory clinic. Of these, 148 were excluded because they were in the pretransplant period, and 87 due to other causes, as described in Figure 1. Thus, 125 participants who performed all assessments were included in this study. We performed a sample size calculation according to an equation proposed by Miot [20]. Considering that 212 KTPs were attended at the kidney disease ambulatory clinic in the data collection period, at least 124 individuals needed to be included in the present study to provide reliable results. The research was approved by Federal University of Uberlandia Research Ethics Committees. All participants signed an informed consent term.

Anthropometric parameters

Current body weight was measured by a portable digital scale (Líder, Aracatuba, Brazil); pretransplant weight was self-reported by participants. Height was measured by a vertical mobile stadiometer (Welmy, Santa Barbara do Oeste, Brazil). Waist circumference (WC) was measured with a non-elastic tape Cescorf positioned at the midway point between the last rib and the iliac crest. Three measurements were performed and the mean value was considered. All measurements were performed according to Lohman's protocol [21]. Body mass index (BMI) was calculated by dividing the body weight (current or pretransplant) by height squared.

Body composition

Body composition evaluation was performed using Biodynamics 450 bioimpedance (Biodynamics, Seattle, WA, USA). Ensuring an adequate hydration, participants were asked to avoid the intake of caffeine, alcoholic consumption, and intense physical activity 1 d before the test. They were asked to perform a 12-h overnight fast before the test. The assessment was performed outside the menstrual period for women of childbearing age. Patients were advised to empty their urinary bladders 30 min before the evaluation. Participants remained in the supine position for 5 min before the test to ensure a balance of body fluids. Heart Beat (HeartBeat, Biotronik Comercial Medica Ltd., Sao Paulo, Brazil) electrodes were positioned on the right side of the body at the wrist, hand, ankle, and foot after each site was cleaned with alcohol [22].

Appendicular skeletal muscle mass (ASMM) in kilograms was estimated by Sergi et al. equation [23]. Appendicular skeletal muscle index (ASMI) was calculated. The ASMI consists of ASMM in kilograms divided by the height squared in meter [1]. Body fat mass was estimated by the Segal et al. equation [24].

Strength and functional capacity

Strength was assessed by handgrip strength (HGS). The HGS was measured using a hydraulic hand dynamometer Jamar (Sammons Preston, Rolyon, Bolingbrook, IL, USA). Participants were in a seated position with the adducted arm in neutral rotation, flexed elbow at 90 degrees, to squeeze the dynamometer with maximum power, and the highest value was considered [25].

Functional capacity was evaluated by the 4-m walking test. Six meters were marked on the ground with a tape (1 m to the acceleration zone, 4 m that was counted, and 1 m to the deceleration zone). Participants were positioned with their toes touching the starting line (acceleration zone) and they were told to walk as per their usual gait speed during daily activities. All participants received a voice command from the evaluator to start the test. The walking test was repeated without rest and the attempt performed in a shorter time was considered to calculate the speed in meters per second.

Sarcopenia diagnosis

Sarcopenia diagnosis was performed according to the revised European consensus on definition and diagnosis of sarcopenia [1]. Individuals presenting low HGS (<27 for men and <16 kg for women) plus low ASMI (<7 2for men and <5.5 kg/m2 for women) were considered to have sarcopenia [1,26]. Patients who additionally presented low functional capacity (4-m walking test 0.8 m/s) were considered to have severe sarcopenia [1]. In the present study, individuals presenting all the sarcopenia components in normal range values and who had probable sarcopenia (only low HGS) [1] were included in the non-sarcopenic group. Those individuals who presented sarcopenia or severe sarcopenia were included in the sarcopenic group.

Dietary assessment

Two 24-h food recalls were applied, one in a face-to-face interview and another by phone. These food recalls were performed with an interval of 6 to 10 d, which allowed for the evaluation of the habitual dietary intake and eventually dietary fluctuations. Trained nutritionists carried out the interview using the fivestep multiple-pass method, which consists in a quick list, forgotten foods list, time and occasion, detail and review, and final probe [27]. Dietary data were analysed and calculated using the Nutrition Data System for Research (NDSR). The NDSR evaluated the consumption of energy (kcal), carbohydrates, protein (total and from animal and vegetable food sources), total fat, saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), polyunsaturated fatty acids (PUFAs, and ω-3 (g) and ω-6 (g). Potential misreporting of dietary energy intake was estimated using the Kelly et al. equation [28].

Physical activity levels

The short version of International Physical Activity Questionnaires (IPAQ) validated for the Brazilian population was applied to evaluate the physical activity level (PAL) [29]. IPAQ was applied referring to the last week information, which consisted in evaluating the frequency, duration, and vigorousness of physical activities.

Biochemical parameters

The participant's blood samples were collected after a 12-h overnight fast on the same day that the bioimpedance evaluation was performed. Creatinine was measured by colorimetric method and urea by enzymatic kinetics. C-reactive protein (CRP) levels were measured by immunoturbidimetric method. Glomerular filtration rate (GFR) was estimated by the Chronic Kidney Disease Epidemiology Collaboration Equation [30].

Statistical analysis

The Kolmogorov Smirnov test was performed to analyze the normality of the data. Continuous variables with normal distribution were described as mean and SD, whereas continuous variables with nonparametric distribution were described as median, minimum, and maximum values. Categorical variables were shown as percentage. Student's t test was used for parametric variables and Mann Whitney for nonparametric variables to compare the participants according to the presence of sarcopenia. x^2 test was used to compare the data in percentage between sarcopenic and non-sarcopenic participants. Multiple linear regression analysis was performed to verify whether dietary variables could predict the sarcopenia components. Dietary components (independent variables) were individually inserted in the model with the confounder's variables to evaluate the prediction of the variances of ASMI, HGS, and walking speed (dependent variables). The R^2 value of each statistical model was generated and then a second analysis was performed removing the dietary component from the model. The difference between the R^2 values of the two models was used to estimate the prediction of ASMI, HGS, and walking speed values by dietary components in an isolated form.

Logistic regression analysis was performed to evaluate the odds of having low ASMI, HGS, walking speed, and sarcopenia according to dietary intake. These associations were performed in two models: model 1 was the crude model and model 2 was adjusted for sex, age, body weight, WC, energy intake, GFR, physical activity,

CRP, use of immunosuppressive and corticosteroid drugs (calcineurin inhibitor, cell proliferation and mTOR inhibitors, and prednisone), and misreporting. These analyses were performed using STATISTICA 6.0 (StatSoft, Tulsa, OK, USA) and MedCalc 11.1 (Medcalc, Mariakerke, Belgium) software, and the significance value adopted was $P < 0.05$.

Results

Table 1 shows the characteristics of the participants according to sarcopenia classification. Compared with the individuals who did not have sarcopenia, the patients with sarcopenia had lower current and pretransplant body weight and BMI; lower WC, fat mass, ASMM, ASMI, HGS, and GFR. These individuals ingested less carbohydrate (g and %), total fat (%), MUFA (%), and PUFA (%). However, sarcopenic individuals ingested more protein in g/kg, with no differences between the groups for protein intake in grams. The other variables did not differ according to the sarcopenia classification.

Table 2 shows the linear regression analysis of sarcopenia components with dietary variables. Intake of ω-3 was positively associated with ASMI (kg/m2), predicting 3.26% of its variances. None of the other dietary components were associated with ASMI. Walking speed and HGS were not associated with dietary variables.

Higher intake of carbohydrates (g) and protein (g/kg) increased the chance of having low ASMI in the crude model. However, after adjustments for confounders, these associations were no longer significant. The greater intake of PUFA (g and %) and ω-3 (g) was associated with lower chance to present low ASMI (model 2). Individuals ingesting more carbohydrates (%) were associated with higher odds of having low walking speed in the crude model; however, this association was not significant after adjustments (model 2). None of the dietary components were associated with walking speed and HGS after adjustments for confounders (Table 3).

Table 4 shows the odds to present with sarcopenia according to dietary intake. Greater intake of carbohydrates (g) and protein (g/kg) increased the chance to have sarcopenia; although intake of total fat and PUFA (%) were associated with lower odds of having sarcopenia in the crude model. However, after adjustments for confounders, only the association between intake of PUFA (%) and sarcopenia remained significant.

In addition, after adjustments (model 2), we also observed that greater PUFA (g) and ω-3 (g) intakes decreased the odds of having sarcopenia. Thus, individuals ingesting greater amounts of PUFAs (g and %) had 1.13 to 1.5 lower chance of having sarcopenia, whereas those ingesting more ω-3 had 1.81 lower chance of having sarcopenia. The other dietary variables were not associated with sarcopenia (Table 4).

Discussion

The main finding of present study was that KTPs ingesting more ω-3 and PUFAs presented a lower chance of having sarcopenia and low ASMI, but no associations were observed between dietary intake and muscle strength/function. These results show that the intake of PUFAs and ω-3 seem to be a protective factor for sarcopenia mainly due to the associations with appendicular muscle mass (which is the second sarcopenia component), but not due to muscle strength and functional capacity (first and third sarcopenia components, respectively).

In the present study, we observed that the KTPs with greater intake of ω-3 had 1.8 lower chance (odds ratio [OR], 0.55; 95% confidence interval [CI], 0.45-0.93) of having sarcopenia. To the best of our knowledge, this is the first study to demonstrate that intake of ω-3 can be a protective factor for sarcopenia in KTPs. There are a limited number of studies associating ω-3 intake with sarcopenia, which were carried out in older adults [18,31]. ter Borg et al. [18] observed that older adults with sarcopenia ingest lower amounts of ω-3, which shows that this nutrient can be a possible protective factor for loss of muscle and strength induced by aging. There are several causes for sarcopenia induced by aging, such as hormonal changes, increased inflammation, lack of physical activity, anabolic resistance, and low protein intake [11]. However, individuals with chronic kidney disease may present additional (or distinct) causes for muscle depletion, such as uremia, medication use, metabolic acidosis, loss of nutrients in dialysis, and increased oxidative stress and inflammation [9]. In this way, the present study shows that intake of ω-3 can be a protective factor for sarcopenia in KTPs, who may have additional causes for sarcopenia. We also observed that greater intake of PUFAs decreased the odds of having sarcopenia. Although PUFAs intake was composed mostly of ω-6, we did not observe associations between ω-6 and

sarcopenia, which shows that the associations between PUFAs and sarcopenia can be explained by the ω-3 content in total PUFA intake.

We also associated sarcopenia components (strength, appendicular muscle mass, and walking speed) in an isolated way with dietary intake. A positive association was observed between ω-3 intake and ASMI; whereas no associations were observed between dietary intake and strength/functional capacity. Currently, the evidence is mixed as to the effects of ω-3 intake on muscle mass, strength, and functional capacity in both younger and older adults [31]. Evaluating only cross-sectional studies, such as ours, there is no study showing significant associations between ω-3 intake and muscle/lean mass [31-33]. Therefore, to our knowledge, this is the first study with a cross-sectional design to observe a significant association between intake of ω-3 and muscle mass. We also observed significant associations between intake of PUFAs and muscle mass, which is in agreement with a study by Reinders et al. [33] that showed that plasma PUFA (which may reflect the dietary pattern of PUFA) was associated with muscle size in older adults. Interestingly, both the present study and the study by Reinders et al. [33] demonstrated a positive association between PUFA intake and muscle mass, even with important differences between the studies, such as type of population evaluated, body composition methods, and forms to assess PUFA intake. It reinforces a possible protective effect of PUFA intake on muscle mass, independent of whether older adults or clinical patients (KTPs) were evaluated.

The exact mechanism by which ω-3 could have an effect on muscle mass is not well known. Individuals with greater ω-3 intake present greater amounts of ω-3 incorporated into cellular membranes, including muscle cells [34]. This incorporation can enhance membrane fluidity, improving uptake of amino acids, making cells more sensitive to muscle protein synthesis [31,35-38]. Another possible mechanism could be related to the anti-inflammatory effects induced by ω-3 intake [38]. Chronic KTPs present higher oxidative stress and pro-inflammatory cytokines than healthy individuals [9], which are important causes of muscle loss and sarcopenia [39]. Therefore, it is possible to suggest that KTPs ingesting more ω-3 might have lower inflammation and oxidative stress, preserving muscle mass.

Although intake of PUFAs and ω-3 were associated with sarcopenia and muscle mass, we did not observe associations of these strength is sex-dependent, being significant only in older men.This result [40] can help to explain the findings of the

present study as we evaluated both men and women and no associations were performed according to the sex. It was not possible to perform these analyses in the present study due to the limited number of individuals evaluated when separated by sex. Therefore, future studies should be performed evaluating the association between ω-3 intake and muscle strength in KTPs separating by sex nutrients with strength and walking speed. To date, two cross-sectional studies evaluated the association between ω-3 intake and strength [33,40]. Reinders et al. [33] observed that ω-3 in plasma was not associated with strength in older adults, which is in agreement with the results of the present study. However, Rossato et al. [40], evaluating 2141 older adults (1119 men and 1022 women), showed that the association between ω-3 intake and muscle strength is sex-dependent, being significant only in older men. This result [40] can help to explain the findings of the present study as we evaluated both men and women and no associations were performed according to the sex. It was not possible to perform these analyses in the present study due to the limited number of individuals evaluated when separated by sex. Therefore, future studies should be performed evaluating the association between ω-3 intake and muscle strength in KTPs separating by sex.

Regarding the association between ω-3 intake and functional capacity, the literature presents limited evidence when cross-sectional studies are evaluated, as this association was evaluated only in older adults [41]. Fougere et al. [41] showed that older adults with a lower percentage of total ω-3 fatty acid content in red cells were not associated with physical function. The results of the present study are in agreement with this study [41], which shows that it seems unlikely that ω-3 intake is associated with physical function, independent of the type of population evaluated. However, due to the limited data in the literature, more studies are needed to evaluate the association between ω-3 intake and functional capacity.

The present study demonstrated that only ω-3 and PUFAs intakes were associated with sarcopenia, whereas all the other dietary components were not. It was expected that protein intake would be the main dietary factor associated with sarcopenia as it is an important macronutrient for muscle mass and muscle function [42,43]. However, we did not find an association between protein intake and sarcopenia and its components. This absence of association possibly can be explained because both sarcopenic and nonsarcopenic groups ingested adequate daily amounts of protein (1.1-1.3 g/kg) for the maintenance of muscle mass [44,45]. The same

rationale can be used to explain the lack of association of other macronutrients with sarcopenia and its components. Both sarcopenic and non-sarcopenic individuals also ingested adequate amounts of carbohydrates and lipids [46].

The present study had some limitations. The cross-sectional design did not allow us to conclude a causal inference between dietary intake and the occurrence of sarcopenia. ASMI was evaluated by bioimpedance using the Sergi et al. equation [23], which was not validated for KTPs. However, because there is no validated equation to estimate muscle mass specifically for KTPs [47], the use of this equation is the main form for estimating ASMI in clinical practice, according to the revised European consensus on definition and diagnosis of sarcopenia [1]. Another limitation is the lack of specific cutoff values for diagnosing sarcopenia in KTPs. To minimize this limitation, we performed linear regression analyses to verify the associations without the use of cutoff values. As strengths, this was the first study to associate dietary intake with sarcopenia and its components in KTPs.

Conclusion

Intake of ω-3 and PUFAs are protective factors for sarcopenia and low muscle mass, but not for strength and functional capacity, in KTPs. Randomized clinical trials are needed to evaluate the possible effects of ω-3 intake on muscle mass, sarcopenia, or both.

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Author contributions and conflict of interest:

ASR, LSL, and HOS wrote the manuscript and participated in collection and analysis of data. EPO carried out the conception and design of the study, participated in the interpretation of the data, and wrote and contributed to the revision of the manuscript. The authors have no conflicts of interest to declare.

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Figures and tables:
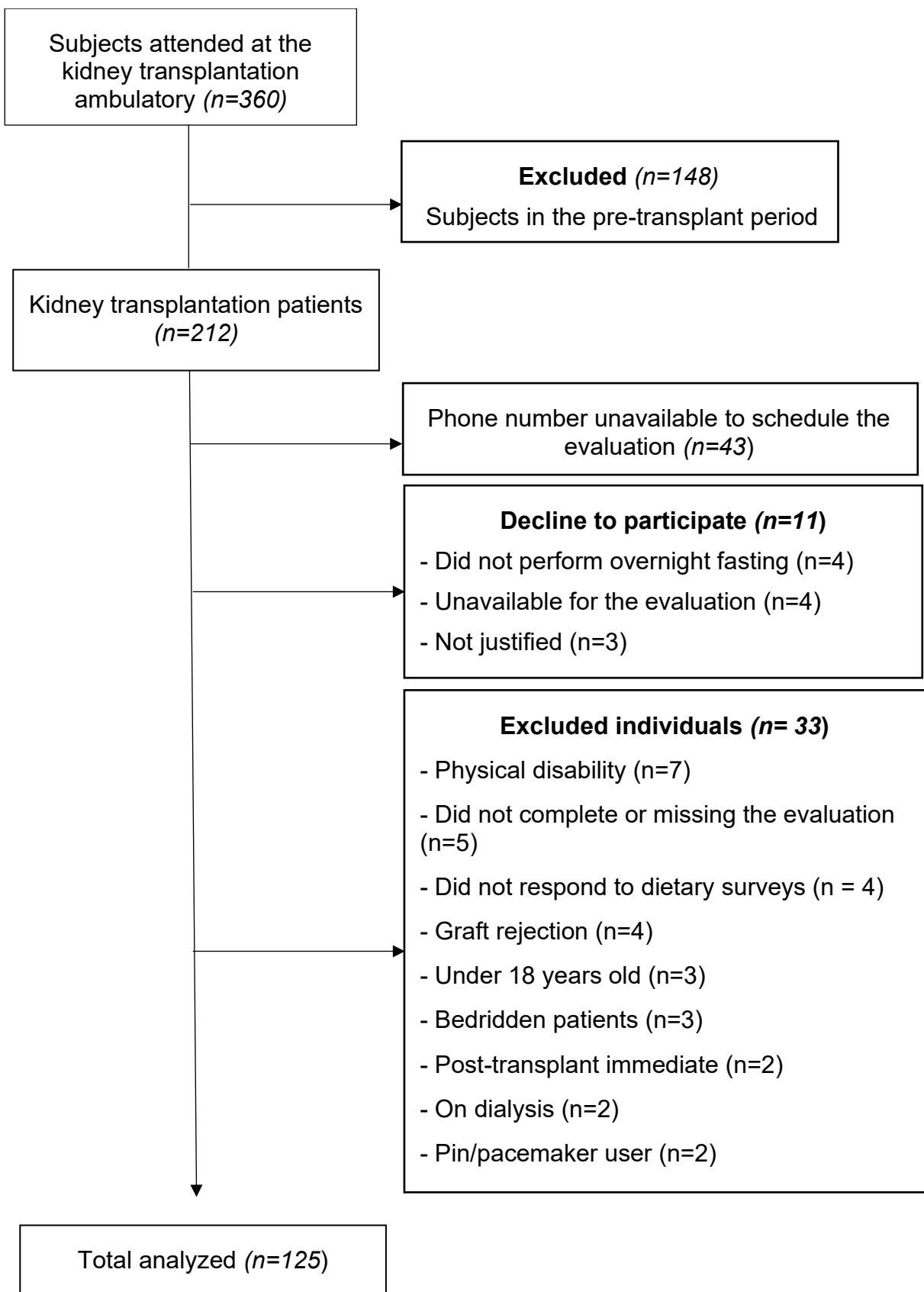
Figure 1. Flow-chart of the participants.

Table 1. Participant's characteristics according to sarcopenia classification.

Variables	All (n = 125)	Sarcopenic (n = 23)	Non Sarcopenic (n= 102)	p-value
Demographic parameters				
Age (y)	48.0 ± 12.0	46.1 ± 14.5	48.5 ± 11.0	0.368
Sex n (%)				
Men	85 (68.0)	19 (82.6)	66 (64.7)	0.096
Women	40 (32.0)	4 (17.4)	36 (35.3)	
Lifestyle				
Smoking n (%)	6.0 (4.8)	3.0 (13.0)	3.0 (2.9)	0.075
Physical Activity (min/week)	120 (0.0 – 900)	100 (0.0 - 780)	145 (0.0 – 900)	0.563
Comorbidities				
Diabetes Mellitus n (%)	30.0 (24.0)	4.0 (17.4)	26.0 (25.5)	0.207
Systemic Arterial Hypertension n (%)	98.0 (78.4)	17.0 (73.9)	81.0 (79.4)	0.153
Anthropometric Parameters				
Current Weight (kg)	70.7 ± 14.2	**56.8 ± 9.9**	**74.5 ± 12.8**	**<0.001**
Pretransplant Weigth (kg)	59.8 ± 12.4	**53.7 ± 7.5**	**61.6 ± 13**	**0.003**
Height (m)	1.64 ± 0.08	1.65 ± 0.07	1.63 ± 0.08	0.306
Current Body Mass Index (kg/m²)	26.3 ± 5.2	**20.7 ± 2.9**	**27.9 ± 4.5**	**0.005**
Pretransplant Body Mass Index (kg/m²)	22.6 ± 4.2	**19.5 ± 2.4**	**23.5 ± 4.2**	**<0.001**
Waist Circumference (cm)	94.9 ± 16.0	**81.1 ± 9.7**	**98.7 ± 15.3**	**<0.001**
Body Composition				
Fat Mass (kg)	27.4±12.1	**22.1 ± 13.8**	**28.9 ± 11.3**	**0.011**
Fat Mass (%)	37.4 ± 10.6	33.5 ± 11.4	38.3 ± 10.3	0.070
Appendicular Skeletal Muscle Mass (kg)	19.2 ± 3.4	**16.5 ± 2.7**	**20.0 ± 3.2**	**<0.001**
Appendicular Skeletal Muscle Index (kg/m²)	7.1 ± 0.9	**6.0 ± 1.5**	**7.5 ± 0.7**	**<0.001**
Physical Performance and Strength				
4-meters walking test (m/s)	1.1 ± 0.2	1.1 ± 0.3	1.1 ± 0.2	0.948
Handgrip Strength (kg)	18.7 ± 10.0	**13.9 ± 6.2**	**20.0 ± 10.5**	**0.004**
Drugs				
Prednisone (mg/d)	5.0 (0.0 – 50.0)	5.0 (0.0 – 50.0)	5.0 (0.0 – 10.0)	0.353
Corticoides drugs, n (%)	115 (92.0)	22.0 (95.7)	93.0 (91.2)	0.475
Calcineurin inhibitor use,* n (%)	81.0 (64.8)	15.0 (65.2)	66.0 (64.7)	0.963
Cell proliferation inhibitor use,† n (%)	105 (84.0)	21.0 (91.3)	84.0 (82.4)	0.290

mTOR inhibitor use,‡ n (%)	25.0 (20.0)	6.0 (26.1)	19.0 (18.6)	0.419
Kidney Transplantation Data				
Urea (mg/dL)	50.7 ± 25.0	52.2 ± 23.5	50.2 ± 23.5	0.706
Creatinine (mg/dL)	1.7 ± 1.1	1.8 ± 1.5	1.6 ± 1.0	0.637
Glomerular Filtration Rate (ml/min/1.73)	61.1 ± 10.1	**50.4 ± 17.6**	**64.0 ± 24.8**	**0.008**
C-Reactive Protein (mg/dL)	0.31 (0.03 – 22.4)	0.20 (0.03 – 11.7)	0.32 (0.03 – 22.4)	0.208
Transplant Time (month)	72.0 (3.0 – 444)	60.0 (3.0 - 336)	76.0 (4.0 - 444)	0.395
Dialysis Time (month)	37.0 (4.0 – 195)	48.0 (5.0 - 195)	36.0 (4.0 - 192)	0.576
Type of Dialysis n (%)				
Peritoneal dialysis	7.0 (5.6)	0.0 (0.0)	7.0 (6.9)	0.339
Hemodialysis	107 (85.6)	20.0 (87.0)	87.0 (85.3)	
Peritoneal dialysis and hemodialysis	11.0 (8.8)	3.0 (13.0)	8.0 (7.8)	
Type of Donor n (%)				
Living	47.0 (37.6)	9.0 (39.1)	38.0 (37.3)	0.867
Deceased	78.0 (62.4)	14.0 (60.9)	64.0 (62.7)	
Number of Transplants n (%)				
1st Transplant	114 (91.2)	20.0 (87.0)	94.0 (92.2)	0.426
2st Transplant	11.0 (8.8)	3.0 (13.0)	8.0 (7.8)	
Dietary Assessment				
Energy (kcal)	1741 ± 576	1717 ± 586	1826 ± 538	0.385
Carbohydrate (g)	212.8 ± 79.6	**205 ± 76.9**	**241 ± 84.2**	**0.035**
Carbohydrate (%)	50.1 ± 9.9	**48.5 ± 9.4**	**52.7 ± 8.6**	**0.026**
Total Protein (g)	84.8 ± 36.5	84.5 ± 31.5	85.8 ± 37.8	0.868
Total Protein (%)	19.8 ± 5.6	19.5 ± 5.5	19.9 ± 5.4	0.751
Protein (g/kg)	1.2 (0.3 – 4.7)	**1.3 (0.6 – 4.7)**	**1.1 (0.3 – 3.0)**	**0.006**
Animal Protein (g)	60.1 ± 34.4	59.1 ± 35.1	60.3 ± 32.7	0.866
Vegetable protein (g)	25.4 ± 9.9	25.3 ± 9.9	25.5 ± 9.9	0.231
Total Fat (g)	60.7 ± 26.0	56.5 ± 23.3	61.9 ± 26.6	0.338
Total Fat (%)	30.1 ± 8.8	**27.2 ± 4.2**	**37.0± 6.4**	**0.048**
Saturated Fatty Acids (g)	18.8 ± 9.0	18.5 ± 9.0	18.9 ± 9.1	0.845
Saturated Fatty Acids (%)	10.7 ± 6.8	10.5 ± 5.4	8.9 ± 3.2	0.137
Monounsaturated Fatty Acids (g)	20.7 ± 9.9	18.4 ± 8.4	21.4 ± 10.2	0.173
Monounsaturated Fatty Acids (%)	10.1 ± 2.8	**9.0 ± 3.1**	**10.8 ± 2.7**	**0.005**
Polyunsaturated Fatty Acids (g)	15.9 ± 8.1	14.5 ± 6.2	16.3 ± 8.5	0.309
Polyunsaturated Fatty Acids (%)	9.2 ± 2.6	**7.0 ± 1.1**	**9.9 ± 1.6**	**0.047**

Omega-3 (g)	1.4 (0.5 – 4.9)	1.4 (0.5 – 2.3)	1.4 (0.7 – 4.9)	0.258
Omega-6 (g)	13.9 ± 7.2	12.6 ± 5.5	14.3 ± 7.6	0.287
Misreporting (%)	16.4 ± 5.7	16.2 ± 5.9	17.3 ± 5.4	0.385

Sarcopenia: Low handgrip strength plus low appendicular skeletal muscle mass index if low walk speed (severe sarcopenia).

*Calcineurin inhibitor: tacrolimus or cyclosporine.†Cell proliferation inhibitor: azathioprine, mycophenolate sodium, and mycophenolate mofetil.‡mTOR inhibitors: everolimus and sirolimus.

Table 2. Linear regression analysis of sarcopenia components with dietary variables.

	Beta	R² %	**R² %	p
**Appendicular Skeletal Muscle Index (kg/m²)**				
Carbohydrate (g)	0.009	65.74	0.00	0.939
Carbohydrate (%)	0.071	66.21	0.47	0.265
Total Protein (g)	- 0.025	65.76	0.02	0.789
Total Protein (%)	0.089	66.46	0.72	0.168
Animal Protein (g)	0.008	65.75	0.01	0.914
Vegetable protein (g)	- 0.046	65.83	0.09	0.195
Protein (g/kg)	- 0.146	66.67	0.93	0.117
Total Fat (g)	0.076	65.88	0.14	0.540
Total Fat (%)	0.094	66.53	0.79	0.148
Saturated Fatty Acids (g)	- 0.049	65.82	0.08	0.639
Saturated Fatty Acids (%)	0.062	66.09	0.35	0.340
Monounsaturated Fatty Acids (g)	0.042	65.80	0.06	0.691
Monounsaturated Fatty Acids (%)	0.082	66.35	0.61	0.205
Polyunsaturated Fatty Acids (g)	0.123	66.49	0.75	0.158
Polyunsaturated Fatty Acids (%)	0.122	67.08	1.34	0.059
Omega-3 (g)	**0.199**	**69.00**	**3.26**	**0.002**
Omega-6 (g)	0.124	66.53	0.79	0.148
**4-meters walking test (m/s)**				
Carbohydrate (g)	- 0.038	26.52	0.56	0.356
Carbohydrate (%)	- 0.176	28.82	2.86	0.059
Total Protein (g)	0.011	25.96	0.00	0.936
Total Protein (%)	- 0.153	28.11	2.15	0.104
Animal Protein (g)	0.031	26.02	0.06	0.783

Vegetable protein (g)	- 0.109	26.52	0.56	0.409
Protein (g/kg)	- 0.040	26.03	0.07	0.770
Total Fat (g)	0.048	26.79	0.83	0.672
Total Fat (%)	- 0.086	26.63	0.67	0.365
Saturated Fatty Acids (g)	0.030	26.78	0.82	0.293
Saturated Fatty Acids (%)	- 0.044	26.13	0.17	0.645
Monounsaturated Fatty Acids (g)	0.032	26.41	0.45	0.386
Monounsaturated Fatty Acids (%)	- 0.093	26.73	0.77	0.331
Polyunsaturated Fatty Acids (g)	0.196	27.88	1.92	0.125
Polyunsaturated Fatty Acids (%)	- 0.107	26.99	1.03	0.260
Omega-3 (g)	0.006	25.97	0.01	0.950
Omega-6 (g)	0.193	27.86	1.90	0.127
Handgrip Strength (kg)				
Carbohydrate (g)	- 0.055	45.46	0.08	0.780
Carbohydrate (%)	0.150	47.50	2.12	0.060
Total Protein (g)	0.080	45.67	0.29	0.496
Total Protein (%)	0.175	46.17	0.79	0.304
Animal Protein (g)	0.039	45.48	0.10	0.689
Vegetable protein (g)	0.089	45.76	0.38	0.433
Protein (g/kg)	- 0.040	45.46	0.08	0.736
Total Fat (g)	0.009	45.39	0.01	0.955
Total Fat (%)	0.134	46.99	1.61	0.103
Saturated Fatty Acids (g)	0.031	45.42	0.04	0.813
Saturated Fatty Acids (%)	0.164	47.80	2.42	0.054
Monounsaturated Fatty Acids (g)	- 0.033	45.43	0.05	0.806
Monounsaturated Fatty Acids (%)	0.079	45.96	0.58	0.334

Polyunsaturated Fatty Acids (g)	0.013	45.40	0.02	0.906
Polyunsaturated Fatty Acids (%)	0.136	47.06	1.68	0.095
Omega-3 (g)	0.120	46.57	1.19	0.162
Omega-6 (g)	0.006	45.40	0.02	0.957

* Adjusted for sex, age, weight, waist circumference, energy intake, glomerular filtration rate, physical activity , C-reactive protein, use of immunosuppressive and corticoids drugs: calcineurin inhibitor, cell proliferation and mTOR inhibitors, prednisone and caloric intake misreporting.
**R^2: Is the difference between the R^2 independent variable + adjusts and only R^2 adjusted fixed without variable.R^2 without dietary variables:

Table 3. Logistic regression analysis of sarcopenia components with dietary variables.

	Model 1		Model 2	
	OR	CI (95%)	OR	CI (95%)
Low Appendicular Skeletal Muscle Mass Index				
Carbohydrate (g)	**1.05**	**(1.03 – 1.11)**	1.01	(0.99 – 1.03)
Carbohydrate (%)	0.99	(0.98 – 1.07)	0.99	(0.97 – 1.01)
Total Protein (g)	1.01	(0.99 – 1.12)	0.98	(0.96 – 1.01)
Total Protein (%)	0.97	(0.92 – 1.02)	0.94	(0.85 – 1.04)
Animal Protein (g)	0.99	(0.98 – 1.15)	0.99	(0.97 – 1.01)
Vegetable Protein (g)	1.02	(0.98 – 1.06)	0.98	(0.89 – 1.09)
Protein (g/kg)	**2.3**	**(1.22 – 4.44)**	0.84	(0.25 – 2.79)
Total Fat (g)	0.99	(0.97 – 1.02)	0.96	(0.91 – 1.01)
Total Fat (%)	0.90	(0.84 – 0.97)	0.92	(0.82 – 1.02)
Saturated Fatty Acids (g)	1.01	(0.96 – 1.05)	1.01	(0.89 – 1.11)
Saturated Fatty Acids (%)	0.98	(0.94 – 1.02)	0.94	(0.83 – 1.07)
Monounsaturated Fatty Acids (g)	0.90	(0.79 – 1.02)	0.90	(0.79 – 1.02)
Monounsaturated Fatty Acids (%)	0.79	(0.66 – 0.93)	0.82	(0.63 – 1.06)
Polyunsaturated Fatty Acids (g)	0.99	(0.94 – 1.04)	**0.88**	**(0.76 – 0.91)**
Polyunsaturated Fatty Acids (%)	**0.85**	**(0.81 – 0.89)**	**0.70**	**(0.46 – 0.97)**
Omega-3 (g)	0.83	(0.50 – 1.41)	**0.09**	**(0.04 – 0.60)**
Omega-6 (g)	0.98	(0.93 – 1.04)	0.96	(0.87 – 1.06)
Low walk speed				
Carbohydrate (g)	1.02	(0.99 – 1.01)	1.05	(0.99 – 1.11)
Carbohydrate (%)	**1.02**	**(1.01 – 1.14)**	1.01	(0.99 – 1.03)
Total Protein (g)	0.98	(0.96 – 1.10)	0.98	(0.92 – 1.05)

Total Protein (%)	0.96	(0.98 – 1.01)	1.05	(0.99 – 1.12)
Animal Protein (g)	0.97	(0.95 – 1.10)	0.97	(0.91 – 1.04)
Vegetable protein (g)	1.02	(0.95 – 1.07)	1.26	(0.92 – 1.70)
Protein (g/kg)	0.36	(0.09 – 1.38)	1.16	(0.03 – 39.90)
Total Fat (g)	0.97	(0.94 – 1.01)	0.78	(0.57 – 1.07)
Total Fat (%)	1.01	(0.99 – 1.03)	1.03	(0.99 – 1.30)
Saturated Fatty Acids (g)	0.90	(0.81 – 1.09)	0.89	(0.99 – 1.11)
Saturated Fatty Acids (%)	1.03	(0.96 – 1.10)	1.06	(0.94 – 1.20)
Monounsaturated Fatty Acids (g)	0.95	(0.88 – 1.03)	0.75	(0.53 – 1.04)
Monounsaturated Fatty Acids (%)	1.03	(0.97 – 1.08)	1.09	(0.97 – 1.21)
Polyunsaturated Fatty Acids (g)	0.99	(0.83 – 1.19)	0.93	(0.84 – 1.03)
Polyunsaturated Fatty Acids (%)	1.06	(0.99 – 1.13)	1.13	(0.99 – 1.30)
Omega 3(g)	0.65	(0.27 – 1.60)	1.37	(0.42 – 4.36)
Omega 6 (g)	0.92	(0.82 – 1.05)	0.91	(0.75 – 1.11)
Low Handgrip Strength				
Carbohydrate (g)	0.99	(0.99 – 1.04)	1.01	(0.98 – 1.14)
Carbohydrate (%)	0.99	(0.98 – 1.18)	0.99	(0.98 – 1.20)
Total Protein (g)	0.99	(0.98 – 1.04)	0.99	(0.97 – 1.01)
Total Protein (%)	0.98	(0.96 – 1.03)	0.97	(0.94 – 1.01)
Animal Protein (g)	0.94	(0.98 – 1.05)	0.99	(0.97 – 1.15)
Vegetable protein (g)	0.97	(0.94 – 1.02)	0.98	(0.91 – 1.05)
Protein (g/kg)	1.02	(0.54 – 1.85)	1.24	(0.32 - 4.81)
Total Fat (g)	0.99	(0.97 – 1.09)	1.03	(0.96 – 1.04)
Total Fat (%)	0.98	(0.97 – 1.03)	0.98	(0.96 – 1.01)
Saturated Fatty Acids (g)	0.97	(0.93 – 1.03)	1.02	(0.92 – 1.10)
Saturated Fatty Acids (%)	0.94	(0.89 – 1.03)	0.95	(0.89 – 1.02)

Monounsaturated Fatty Acids (g)	0.98	(0.94 – 1.03)	1.01	(0.91 – 1.10)
Monounsaturated Fatty Acids (%)	0.97	(0.93 – 1.02)	0.97	(0.92 – 1.02)
Polyunsaturated Fatty Acids (g)	0.99	(0.94 – 1.04)	1.01	(0.91 – 1.10)
Polyunsaturated Fatty Acids (%)	0.95	(0.90 – 1.01)	0.95	(0.88 – 1.02)
Omega-3 (g)	0.83	(0.54 – 1.29)	0.78	(0.38 – 1.62)
Omega-6 (g)	0.99	(0.94 – 1.05)	1.01	(0.91 – 1.17)

Model 1: Crude. **Model 2:** Adjusted for sex, age, weight, waist circumference, energy intake, glomerular filtration rate, physical activity , C-reactive protein, use of immunosuppressive and corticoids drugs: calcineurin inhibitor, cell proliferation and mTOR inhibitors, prednisone and caloric intake misreporting.

Table 4. Logistic regression analysis of sarcopenia with dietary variables.

	Model 1		Model 2	
	OR	CI (95%)	OR	CI (95%)
Carbohydrate (g)	**1.01**	**(1.01 – 1.11)**	1.01	(0.99 – 1.03)
Carbohydrate (%)	0.99	(0.98 – 1.07)	0.99	(0.97 – 1.01)
Total Protein (g)	1.01	(0.98 – 1.01)	0.98	(0.96 – 1.01)
Total Protein (%)	0.96	(0.91 – 1.02)	0.93	(0.83 – 1.03)
Animal Protein (g)	0.99	(0.98 – 1.01)	0.99	(0.96 – 1.01)
Vegetable protein (g)	1.02	(0.98 – 1.06)	0.99	(0.90 – 1.09)
Protein (g/kg)	**2.33**	**(1.2 – 4.40)**	0.83	(0.24 – 2.76)
Total Fat (g)	0.99	(0.97 – 1.01)	0.96	(0.91 – 1.01)
Total Fat (%)	**0.90**	**(0.83 – 0.97)**	0.92	(0.83 – 1.03)
Saturated Fatty Acids (g)	0.99	(0.94 – 1.04)	1.01	(0.90 – 1.11)
Saturated Fatty Acids (%)	0.90	(0.79 – 1.03)	0.95	(0.84 – 1.08)
Monounsaturated Fatty Acids (g)	0.96	(0.92 – 1.01)	0.90	(0.80 – 1.02)
Monounsaturated Fatty Acids (%)	0.79	(0.66 – 0.94)	0.84	(0.66 – 1.06)
Polyunsaturated Fatty Acids (g)	0.98	(0.92 – 1.04)	**0.88**	**(0.75 – 0.96)**
Polyunsaturated Fatty Acids (%)	**0.80**	**(0.64 – 0.94)**	**0.65**	**(0.46 – 0.94)**
Omega-3 (g)	0.55	(0.54 – 1.24)	**0.55**	**(0.45 – 0.93)**
Omega-6 (g)	0.96	(0.89 – 1.03)	0.97	(0.87 – 1.07)

Model 1: Crude. **Model 2:** Adjusted for sex, age, weight, waist circumference, energy intake, glomerular filtration rate, physical activity , C-reactive protein, use of immunosuppressive and corticoids drugs: calcineurin inhibitor, cell proliferation and mTOR inhibitors, prednisone and caloric intake misreporting.

Artigo 2. Artigo intitulado "***Association of the number of meals containing at least 20 and 30 grams of protein with muscle mass, strength and functional capacity in kidney transplant patients***", que será submetido à revista *European Journal of Clinical Nutrition* (Impact Factor = 4.016).

Association of the number of meals containing at least 20 and 30 grams of protein with muscle mass, strength and functional capacity in kidney transplant patients

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ABSTRACT

Aim: To associate the number of meals containing at least 20 and 30 grams of protein with muscle mass, muscle strength and functional capacity in kidney transplant patients (KTPs). **Methods:** Cross-sectional study with 123 KTPs. Two 24-h recalls were performed. Appendicular skeletal muscle mass (ASMM) was estimated using Sergi et al. equation (2015). Appendicular skeletal muscle mass index (ASMI) was calculated. Handgrip strength (HGS) test, balance test, five times sit to stand test (5STS), short physical performance battery (SPPB) and the 4-m walking test were performed. Analyses were performed for total sample and sub-analyses by age ($\geq$ 50 and < 50). **Results:** Number of meals containing at least 30 grams of protein was negatively associated with time to perform 5STS (Beta = - 0.446; p = 0.023) and was positively associated with SPPB score (Beta = 0.421; p = 0.037) among KTPs aged $\geq$ 50 years. In these subanalyses there was no association with ASMI (Beta =0.114; p =0.510); HGS (Beta = 0.043; p = 0.814); balance test (Beta = 0.044; p = 0.808) and 4-m walking test (Beta = -0.010; p = 0.955). Number of meals with at least 20 g of protein was not associated with any of muscle parameters in these subanalyses. In analyses with total sample and with participants < 50, no associations were observed between the number of meals with 20 and 30 grams of protein and muscle mass, strength and functional capacity. **Conclusions:** Number of meals containing at least 30 grams of protein is associated with better performance on 5STS and SPPB among KTPs aged $\geq$50.

Keywords: Food Consumption; Kidney Transplantation; Muscle Strength; Muscle; Physical Functional Performance.

INTRODUCTION

Several etiological factors are related to the loss of muscle mass and impaired strength and functional capacity/physical performance in individuals with chronic kidney disease (CKD). These factors can be divided into factors that reduce protein synthesis and that increase protein breakdown, resulting in a negative protein balance. Among the factors that reduce protein synthesis, there are reduced appetite and dietary restrictions of conservative treatment, aging, sedentary lifestyle, reduced stimulus for muscle regeneration, reduced energy and protein intake on dialysis days, in addition to amino acid loss in dialysate. Factors that can increase protein degradation include inflammation, insulin resistance, metabolic acidosis and oxidative stress. The loss of muscle mass caused by negative protein balance results in loss of muscle strength, poor physical performance, disability and frailty (1).

Kidney transplant is considered the best treatment for individuals with end-stage CKD, but to minimize the risk of rejection, after transplant it is necessary to use immunosuppressive drugs for life. A recent study showed that quality of life and muscle strength of patients after six months of kidney transplant improved compared to the pre-transplant period, regardless of the high doses of immunosuppressive drugs used (2). However, despite this improvement, the participants remained with unsatisfactory muscle strength and quality of life. In fact, previous studies carried out by our research group showed that sarcopenia and low muscle strength and poor physical performance in functional capacity tests are prevalent in kidney transplant patients (KTPs) (3-5).

Adequate protein intake is one of the main factors related to preservation of muscle mass, muscle strength and functional capacity, as well as to prevent the development of sarcopenia, frailty and disability (6-8). In this sense, it has been suggested that, in addition to the total daily protein intake, other characteristics such as protein quality, the distribution of its consumption throughout the day and the dose of protein per meal may be involved in the maintenance of muscle mass, strength and functional capacity (9, 10). Thus, a recommendation for consumption of 0.25 - 0.3 g/kg of protein per meal for adults and 0.4 g/kg of protein per meal for older adults was proposed (around 20 to 40 grams of protein per meal for adults and older adults, respectively) as ideal for promoting maximum protein synthesis (11). However, as these recommendations were drawn from myofibrillar protein synthesis data (which does not necessarily correspond to muscle mass) (12), it is not clear whether adequate

protein intake per meal is associated with greater muscle mass, greater muscle strength or greater performance physical/functional capacity.

Some studies carried out with older adults have evaluated the association of protein distribution throughout the day and/or the adequacy of the protein dose per meal with lean mass (13-15), muscle mass (15), muscle strength and functional capacity (16), with conflicting results. Some of these studies (13-15) found positive associations, while other did not (16). These studies in the elderly show conflicting results, furthermore we evaluated this in a clinical population of kidney transplant patients who have been using immunosuppressive and corticosteroid drugs for many years and who suffered all the negative effects of CKD on their protein metabolism as mentioned above. To the best of our knowledge, no studies were found that associated the pattern of protein consumption throughout the day and/or the adequacy of the protein dose per meal with functional capacity and muscle strength in clinical populations such as KTPs. Therefore, the aim of the present study was to associate the number of meals containing at least 20 and 30 grams of protein with muscle mass, muscle strength and functional capacity variables in KTPs.

METHODS

Study design and participants

A cross-sectional study was carried, evaluating KTPs at kidney transplantation ambulatory clinic of the Federal University of Uberlandia, Minas Gerais State, Brazil. Age greater than or equal to 18 years and minimum of 3 months of kidney transplantation were the inclusion criteria. Participants who were unable to answer the questions and/or to perform the body composition or functional capacity evaluation, KTPs on dialysis, and kidney graft rejection and/or failure and participants who did not respond to dietary intake recalls were excluded from the study. In all, 360 patients were attended at the kidney transplantation ambulatory clinic. Of these, 148 were excluded because they were in the pretransplant period, and 89 due to other causes, as described in Figure 1. Thus, 123 participants who performed all assessments were included in this study. The study protocol was approved by the Federal University of Uberlandia Research Ethics Committees (protocol number: 1688246) and all patients signed the consent form. The power of the sample size was calculated *a posteriori* using G* Power software version 3.1.9.2. For the total sample: Statistical test: Linear multiple regression: Fixed model, single regression coefficient; Post hoc. Input: Tail(s):

Two; Effect size f²: 0.3; α err prob: 0.05; Total sample size: 123; Number of predictors:9. Output: Power (1-β err prob): 0.99. For the sub-sample of individuals aged 50 years and over: Statistical test: Linear multiple regression: Fixed model, single regression coefficient; Post hoc. Input: Tail(s): Two; Effect size f²: 0.3; α err prob: 0.05; Total sample size: 59; Number of predictors: 9. Output: Power (1-β err prob): 0.98. For the sub-sample of individuals with less than 50 years old: Test family: t tests. Statistical test: Linear multiple regression: Fixed model, single regression coefficient; Post hoc. Input: Tail(s): Two; Effect size f²: 0.3; α err prob: 0.05; Total sample size: 64; Number of predictors: 9. Output: Power (1-β err prob): 0.99.

Demographic data, information on CKD and kidney transplant, comorbidities and medicine use

Firstly, an anamnesis was performed to verify sociodemographic information, such as age and sex, medicine use, previous disease, comorbidities and information about kidney disease. Kidney disease questionnaire included the information of the chronic disease, dialysis time and kidney transplantation duration, and the donor type (living or deceased).

Anthropometric parameters

Current body weight was measured by a portable digital scale with precision of 100 g (Lıder, Araçatuba, Brazil) and height by a vertical mobile stadiometer with 0.1 cm precision scale (Welmy, Santa Barbara do Oeste, Brazil). Pretransplant weight was self-reported by participants. Waist and calf circumferences were measured with a non-elastic tape Cescorf® (Cescorf, Porto Alegre, Brazil). Three measurements were performed and the mean value was considered. All measurements were performed according to Lohman's protocol (17).

Body composition and Phase Angle (PhAº)

Body composition and PhAº evaluation were performed using Biodynamics 450 bioimpedance (Biodynamics, Seattle, WA, USA). Patients were evaluated after 12-hour overnight fast and were advised to maintain an adequate hydration, and for this were asked to avoid the intake of caffeine, alcoholic consumption, and intense physical activity one day before the test. The assessment was performed outside the menstrual period for women of childbearing age. Patients were advised to empty their urinary bladders 30 min before the evaluation and remained in the supine position for 5 min

before the test to ensure a balance of body fluids. Electrodes (HeartBeat, Biotronik Comercial Medica Ltda., Sao Paulo, Brazil) were positioned on the wrist, hand, ankle, and foot on the body right side (18). Body water values were considered acceptable when it corresponded between 69% and 75% of total body water per lean mass, according to the manufacturer's recommendations. Appendicular skeletal muscle mass (ASMM) in kilograms was estimated using Sergi et al. equation (19). Appendicular skeletal muscle mass index (ASMI) was calculated, which consists of appendicular skeletal muscle mass (kg) divided by height squared (m²) (20). Fat body mass was estimated using the equation of Segal et al (21).

Strength and functional capacity

The handgrip strength (HGS) test and the five times sit to stand test (5STS) were performed to assess the muscle strength (20). A calibrated hand dynamometer Jamar® (Sammons Preston, Rolyon, Bolingbrook, IL) was used to measure the HGS. Participants were positioned seated with the adducted arm in neutral rotation, flexed elbow at 90, with forearm and wrist in neutral rotation, according to the American Society of Hand Therapists (22). Three measurements were performed in the dominant hand with a rest interval of 20 seconds, and the higher value was considered (20). To perform 5STS, the participant was instructed to sit and get up from the chair five times, as fast as possible, being the test time recorded (20, 23). The functional capacity was evaluated using the short physical performance battery (SPPB) and the 4-m walking test (20, 24). The SPPB included balance tests, 4-m walking test and the 5STS, assessed together. Each test had 4 points maximum, which were totalized as 12 points by the end of the test. The balance test has the purpose of evaluating if the participants can stay in three positions for ten seconds each: the feet together, the semi-tandem position and the tandem. The 4 m walk test consists of: 1 m to the acceleration zone, 4 m in which the participant should walk at the usual gait speed they achieve during their daily activities, and 1 m to the deceleration zone. The 4-m walking test was repeated without rest, and the attempt performed in a shorter time was used to calculate the speed in meters per second. Participants received a voice command from the evaluator to start the test (24). Physical performance of the participants in the 4-m walking test was also assessed separately, and was considered low when the speed was ≤ 0.8 m/second (20).

Dietary assessment

Two 24-hour dietary recalls were carried out to assess food intake. The first was performed in a face-to-face interview and the second by phone call. An interval of 6-10 days between each dietary recall was considered to estimate the habitual dietary intake. Trained nutritionists carried out the interview using the five-step multiple-pass method, which consists in a quick list, forgotten foods list, time and occasion, detail and review, and final probe (25). Collected data were analysed and calculated using Nutrition Data System for Research (NDS-R, software version 2014). Categorization of the names of the meals was performed by the participants themselves during the 24-hour dietary recalls in one of the steps of the five-step multiple-pass method. The definition of what was considered a meal was performed by the participant in step 3 of the five steps multiple pass method (time and occasion). Subsequently, the researchers evaluated how many of the daily meals these individuals ingested at least 20 and or 30 g of protein. Potential misreporting of dietary energy intake was estimated using the Kelly et al. equation (26).

Physical activity levels

Short version of the International Physical Activity Questionnaire validated for Brazilian population (27) was used to determine the physical activity level, as previously described (3).

Biochemical parameters

Blood samples were collected after a 12-h overnight fast. Creatinine was measured by colorimetric method and urea by enzymatic kinetics. C-reactive protein (CRP) levels were measured by immunoturbidimetric method. Glomerular filtration rate (GFR) was estimated by the Chronic Kidney Disease Epidemiology Collaboration Equation (CKD-EPI) (28).

Statistical analysis

The Kolmogorov Smirnov test was performed to analyze the normality of the data. Continuous variables with normal distribution were described as mean and SD, whereas continuous variables with nonparametric distribution were described as median and interquartile range. Categorical variables were shown as percentage. Participants were characterized according to the number of daily meals they consumed at least 20 or 30 grams of protein (none, one or two or more). One-way analysis of

variance (ANOVA) with Tukey post-hoc test was performed to compare continuous variables with normal distribution between these categories. Non-parametric data were compared using the Kruskal–Wallis test. Chi-squared (χ^2) test was used to compare data in percentages (categorical variables). Pearson correlation and linear regression analysis were carried out to evaluate the association of the number of meals with at least 20 or 30 grams of protein intake and muscle mass and physical performance/strength (i.e., HGS, balance test, 4-m walking test, 5STS, and the SPPB). The analyses were performed in two models; model 1 (crude analyses), model 2 adjusted for sex, age, waist circumference, energy intake, total protein intake, GFR and physical activity, and model 3 included all the adjustments of model 2 and in addition the use of immunosuppressive and corticosteroid drugs: calcineurin inhibitor, cell proliferation and mTOR inhibitors, prednisone. Confounding variables included in the models were defined with biological reasoning and based on statistical models used in other studies of our research group (3, 4) that were developed with the same database used in this present study. Additionally, the model's collinearity test was performed and it was observed that the tolerance values were above 0.1 for all independent variables of the model and that the variance inflation factor (VIF) values were less than 5.0, meaning that there was no multicollinearity effect between the model variables and that, therefore, multiple linear regression analysis is adequate. The R^2 value of each statistical model was generated and then a second analysis was performed removing the dietary component from the model. The difference between the R^2 values of the two models was used to estimate the prediction of ASMI, HGS, balance test, 4-m walking test, 5STS, and the SPPB by dietary components in an isolated form. Association analyses were performed for the total sample and sub-analyses subdividing the sample by age (greater than or equal to 50 years old [n = 59] and less than 50 years old [n=64]). Stata 14 (StataCorp, College Station, TX, USA) was the statistical software used. *P*-values ≤ 0.05 were considered as significant.

RESULTS

Sample composed of 123 adults and older adults KTPs, and 68.3% of the participants were male (n=84). Table 1 shows characterization of the participants according to the number of daily meals they consumed at least 20 or 30 grams of protein. There was a higher proportion of men compared to women in the categories with the highest number of meals with at least 20 and 30 grams of protein. Individuals

who consumed more meals with at least 20 and 30 grams of protein were taller, had higher SPPB scores, consumed more energy, protein (g, %, g/kg, animal and vegetable), branched chain amino acids (BCAA), leucine, isoleucine, valine and total fat. Additionally, participants who consumed more meals with at least 20 grams of protein also had a higher percentage of cell proliferation inhibitor use and consumption of carbohydrates in grams. On the other hand, individuals who ate more meals with at least 20 and 30 grams of protein had lower values for the adiposity variables (current and pre-transplant weight, fat mass in percentage and in kilograms), less time to perform the 5STS and consumption of lower percentage of carbohydrates. Individuals who ate more meals with at least 20 grams of protein also had smaller waist circumference. For the other variables, no differences were observed. (Table 1).

Table 2 shows results of simple and multiple linear regression analysis between the number of meals containing at least 20 and 30 grams of protein and muscle mass, strength and physical performance variables. In the analyses performed with the total sample, it was observed that the number of meals containing at least 20 grams of protein was negatively associated with the time to perform the 5STS in the simple linear regression model, however, in the multiple linear regression analyses (models 2 and 3), this association disappeared. On the other hand, the number of meals containing at least 20 grams of protein was positively associated with SPPB score, HGS and balance test score in simple linear regression model, but these associations were no longer significant in models 2 and 3 (multiple linear regression). Similarly, the number of meals with at least 30 grams of protein was associated with the time to perform the 5STS and SPPB score in simple linear regression, but in models 2 and 3 these associations disappeared. Number of meals containing at least 20 and 30 grams of protein were not associated with ASMI, HGS, balance test score and 4-m walking test in any of the linear regression models. In the subanalyses with individuals aged 50 years and over, it was observed that the number of meals containing at least 20 grams of protein was not associated with none of the muscle mass, strength and physical performance variables. On the other hand, number of meals with at least 30 grams of protein was negatively associated with the time to perform the 5STS in simple and multiple linear regression models, predicting among 5.94 to 8.69 % of its variances. The number of meals with at least 30 grams of protein was positively associated with SPPB score in all tested models, predicting among 5.98 to 7.72% of its variances. In

these subanalyses, the number of meals containing at least 30 grams of protein was not associated with ASMI, HGS, balance test score and 4-m walking test in any of the models. In the subanalyses with participants under the age of 50 years, no associations were observed between number of meals containing at least 20 grams of protein and muscle mass, strength and physical performance tests. The number of meals containing at least 30 grams of protein was positively associated with HGS in simple linear regression model, but the same could not be observed in the multiple linear regression models. In these subanalyses, number of meals containing at least 30 grams of protein was not associated with ASMI, 5STS, SPPB score, balance test score and 4-m walking test in any of the models (Table 2).

Regarding the Pearson correlation analysis, the same associations described for the linear regression analyses were observed (Supplementary Table 1).

DISCUSSION

The main finding of the present study was that the number of meals containing at least 30 grams of protein was negatively associated with time to realize 5STS and was positively associated with SPPB score among KTPs aged 50 or over years, regardless of confounders (sex, age, waist circumference, energy intake, total protein intake, GFR, physical activity and use of immunosuppressive and corticosteroid drugs), which indicates that those who consumed more meals with at least 30 grams of protein performed better in these two functional capacity tests. The same was not observed for the total sample or for the sub-sample aged under 50 years. Number of meals containing at least 30 grams of protein was not associated with ASMI, HGS, balance test and gait speed on 4-m walking test. In addition, the number of meals containing at least 20 grams of protein was not associated with muscle mass, muscle strength or physical performance in any of the functional capacity tests performed.

Our results can be compared with a recent study that aimed to assess the association between protein intake distribution and muscle strength, physical function and quality of life (29). In this study, the protein consumption pattern was evaluated according to the coefficient of variation (CV) in spread (CV < 0.43), intermediate (CV = 0.43 – 0.62) and pulse (> 0.62). A more spread protein intake during the main meals was related to a higher gait speed, but not with SPPB score, chair rise, HGS and quality

of life. This study is similar to ours in some respects and differs in others. In the aforementioned study, individuals with the spread protein intake pattern (who ingest approximately 20 and 35 g of protein at breakfast, lunch and dinner with a small variation between meals) showed better physical performance in the gait speed test. In our study, however, there was no association between the number of meals with intake of 20 or 30 grams of protein with 4-m walking test, but with the 5STS and SPPB score. Despite differing in terms of physical tests in which there was an association with protein intake, both studies demonstrated that there is a relationship between the pattern of protein intake and functional capacity tests, despite the differences between the studies. Among the differences, we can highlight that the present study evaluated KTPs, while the aforementioned study assessed community-dwelling elderly people. Furthermore, the methodology used to assess the pattern of protein intake was different. In the present study, we evaluated the number of meals in which individuals reached at least 20 or 30 g of protein, and in that study, the CV was used.

Our results diverged from those found by Hayashi et al (15) in their study carried out with pre-frail and frail elderly, as they found correlations between the number of meals with 20 and 30 g of protein and muscle mass variables, but not with the variables of muscle strength and functional capacity tests and in our study the opposite was observed, with correlation with SPPB and 5STS, but not with ASMI. Despite this, the strength of the association was similar to what we found for SPPB with correlations with similar values, they found correlations with r value from 0.16 to 0.47 between the number of meals with at least 20 and 30 g protein and total muscle mass, appendicular muscle mass and vastus lateralis muscle cross-sectional area, while we found correlations with r values from 0.24 to 0.29 between the number of meals containing at least 30 g of protein and the score SPPB in the sub-analyses with participants aged 50 years and over. The fact that these associations only occurred in the subanalyses with older individuals in our study suggests that they may have a greater relationship with age than with the fact that individuals had undergone kidney transplantation.

The present study findings corroborate with results of the work developed by Loenneke et al.(14), because, in that study, there was a positive association between the frequency of consumption of meals with at least 30 g of protein and muscle strength (voluntary peak isokinetic knee extensor strength), since in our research, we found that the consumption of meals with at least 30 grams of protein was associated with a

shorter time to perform the 5STS - test that is considered a proxy of leg strength (20). We emphasize that the form of assessment of food consumption was the same in our study and in the study by Loenneke et al.(14), and that the consumption of more meals with ≥ 30 g of protein seems to have a beneficial association with lower limbs muscle strength, regardless of the legs muscle strength test used and of the assessed population.

Unlike our findings, cohort study conducted by Farsijani (30) et al. demonstrated that more-evenly mealtime distributed protein intakes was associated with a higher muscle strength composite score (HGS, arms and legs strength), but not with mobility composite score (Time Up and Go, 5STS, 4-m walking test, SPPB). However, it is important to highlight that in the study of Farsijani et al (30), intakes of more than one meal containing at least 30 g protein were infrequently observed, since in this study, a even pattern of protein distribution usually meanted intakes of 18, 23, and 23 g/meal in women and 21, 29, and 30 g/meal in men, whereas uneven pattern of protein distribution reflected 8, 21, and 30 g/meal in women and 11, 20, and 41 g/meal in men, on average (30).

In a recently published systematic review that aimed to explore how dietary protein distribution affects muscle mass and/or muscle strength and/or protein turnover in an adult human population it was observed that a stronger association was found for muscle mass, although limited to observational evidence. The association between uniformity of protein intake with muscle strength and protein turnover was weak (31). In fact, in an observational cross-sectional study of pre-frail and frail elderly people, it was observed that the number of meals containing at least 20 and 30 grams of protein were positively associated with total and appendicular lean mass and with the vastus lateralis muscle cross-sectional area, but not with muscle strength, functional capacity, risk of falls and frailty criteria (15). Additionally, in another study conducted by our research group, we found that the number of meals containing at least 20 grams of protein was associated with greater lean body mass in postmenopausal women (13).

Although associations were found between the number of meals containing at least 30 grams of protein and better performance in the 5STS and SPPB tests in our study and these results are reinforced by other cross-sectional studies, which also observed associations between the pattern of consumption distribution protein and better physical performance and/or muscle strength, it is not yet known whether this

intervention can be important to impact the improvement or maintenance of strength and/or physical performance when the total protein consumption is equalized. The randomized clinical trial conducted by Kim et al. demonstrated that muscle strength (HGS and one repetition maximum for knee extension) did not differ after an 8-week intervention with the 1.1 g kg BW/day protein supply in an even (33/33/33%) or a skewed (15/20/65%) distribution. The short intervention period and the small sample were important limitations of the aforementioned randomized clinical trial; therefore, its conclusions need to be analysed with caution. Thus, to the best of our knowledge, there are no consistent results in the literature from intervention studies evaluating different patterns of protein distribution on muscle strength and function. In this sense, more studies are needed, especially in clinical populations such as KTPs.

Kidney transplant patients have characteristics that differ them from the general population, such as the use of immunosuppressive drugs and corticosteroids for life to reduce the risk of graft rejection (1). The use of these drugs, in turn, interferes with muscle mass and can affect muscle strength and functional capacity (32, 33). Additionally, it is possible that these individuals show loss of muscle mass, strength and physical performance and develop sarcopenia before becoming elderly, as observed in previous studies by our research group (3-5). Furthermore, these individuals have lived with CKD for years. In the conservative treatment phase, these patients undergo protein consumption restriction in order to delay the loss of residual renal function. In the dialysis phase, these patients commonly reduce the practice of physical activity, become sedentary and lose nutrients in the dialysate (1, 34). Other characteristics of CKD are uremia, increased of oxidative stress and inflammation (35). Thus, individuals who underwent kidney transplant may have lost muscle mass, strength, physical performance and functional capacity prior to transplant, and these damages can intensify with the continuous use of immunosuppressive drugs and corticosteroids in the post-transplant period. For all these reasons, KTPs are considered a risk group for muscle depletion, reduced muscle strength and physical performance/functional capacity, and development of sarcopenia. Therefore, studies that evaluate dietary associations with possible benefits for the prevention of these disorders are desirable and necessary.

The present study had some limitations. The cross-sectional design does not allow us to determine the cause–effect relationship. Additionally, the nutrients intake

and amount of protein per meal were assessed using 24-hour dietary recall, which has known limitations. However, to minimize these limitations, we applied two 24-hour dietary recalls to estimate the dietary habits and a standardized interview method was used (25). The sample was not representative of kidney transplantation patients in Brazil and 123 KTPs were evaluated in a single-center study and, therefore, the data presented should be interpreted with caution; however, we emphasize that for studies with KTPs with characteristics similar to participants in the present study, it is possible that the data will be compared. Additionally, it is likely that the sample size did not influence our results, since the associations found were significant independent of the number of adjustments. Another limitations was the assessment of body composition through bioimpedance, since it is not the gold standard method for this purpose, moreover, ASMI was estimated through the Sergi et al. equation, which was not validated for KTPs. Although, because there is no validated equation to estimate muscle mass specifically for KTPs (36), the use of this equation is the main form for estimating ASMI in clinical practice, according to the revised European consensus on definition and diagnosis of sarcopenia (20). As strengths, this was the first study to associate the number of meals containing at least 20 and 30 grams of protein with muscle strength and functional capacity variables in KTPs. Although this information is still not enough to propose new nutritional approaches for KTPs, it contributes to the literature, suggesting the need to carry out future intervention studies, and thus, if these data are confirmed through clinical trials, it will be possible to serve as a basis for the creation of new nutritional guidelines for this population. Furthermore, the analyses were adjusted for several important confounders, allowing us to assess the associations rightly.

CONCLUSION

In conclusion, the number of meals containing at least 30 grams of protein was negatively associated with time to realize 5STS and was positively associated with SPPB score among KTPs aged 50 or over years, which indicates that those who consumed more meals with at least 30 grams of protein performed better in these two functional capacity tests. It is important to highlight that for younger people this

association was not observed, even in the case of a population with metabolic alterations such as KTPs. Future randomized clinical trials should assess whether offering meals with at least 30 grams of protein have a beneficial effect on muscle mass, physical performance and functional capacity and muscle strength in KTPs.

Statement of authorship

ASR, LSL and HOS wrote the manuscript, participated in collection and analysis of data; EPO carried out the conception and design of the study, participated in the interpretation of the data, wrote, and contributed to the revision of the manuscript.

Conflict of interest
 None.

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Figures and tables:
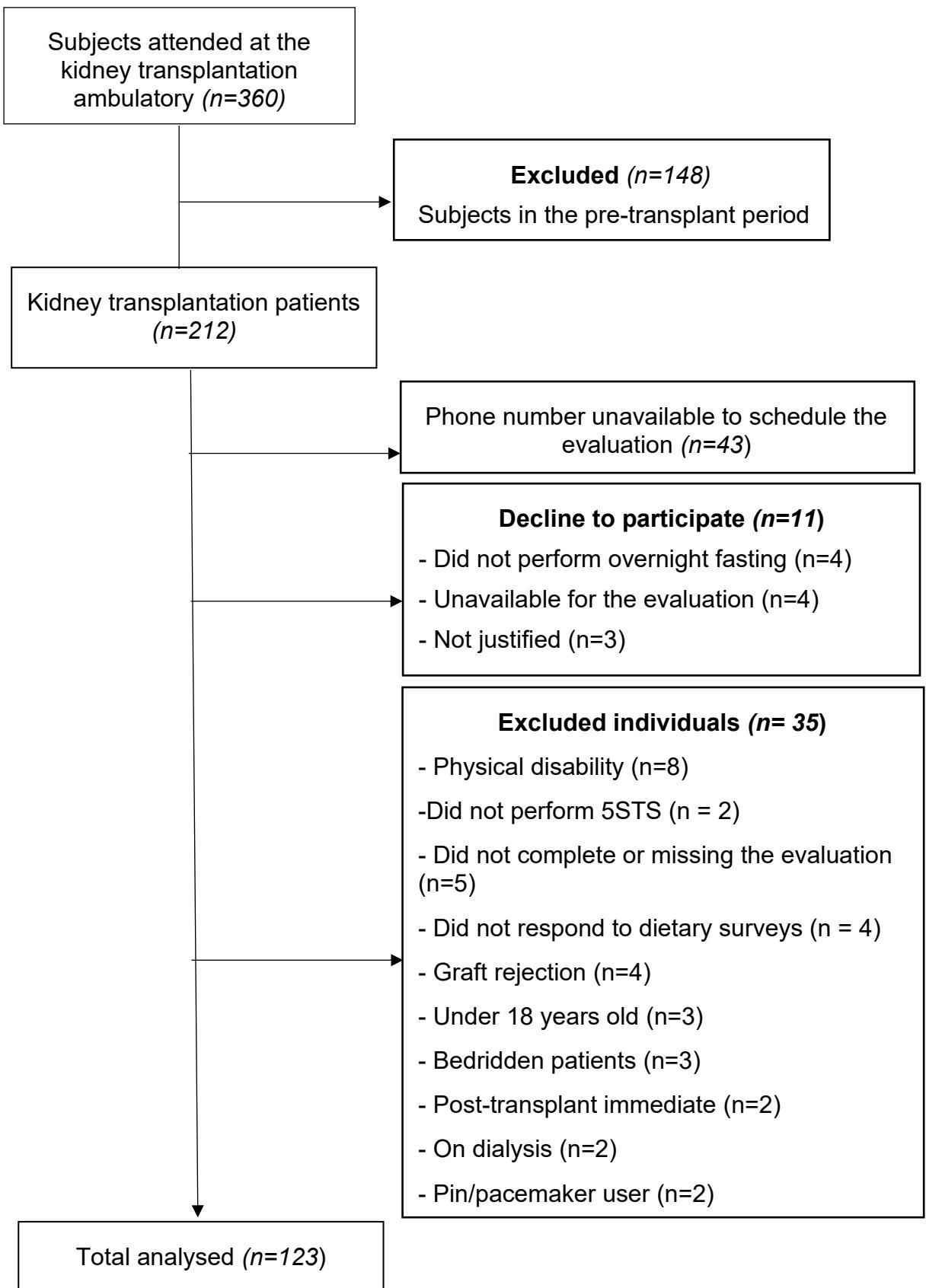
Figure 1. Flow-chart of the participants.

Table 1. Participants characteristics according to number of meals with at least 20 or 30 grams of protein intake.

Variables	Number of meals with ≥ 20 grams of protein				Number of meals with ≥ 30 grams of protein			
	0 (n = 10)	1 (n = 42)	2 or more (n =71)	p	0 (n = 36)	1 (n = 44)	2 or more (n = 43)	p-value
Demographic parameters								
Age (y)	52.8 ± 14.0	47.1 ± 10.6	47.2 ± 12.1	0.344	48.1 ± 14.4	48.7 ± 8.8	46.0 ± 11.9	0.550
Sex, n (%)								
Men	**5.0 (50.0)**	**23.0 (54.8)**	**56.0 (78.9)**	**0.012**	**19.0 (52.8)**	**30.0 (68.2)**	**35.0 (81.4)**	**0.025**
Women	**5.0 (50.0)**	**19.0 (45.2)**	**15.0 (51.1)**		**17.0 (47.2)**	**14.0 (31.8)**	**8.0 (18.6)**	
Comorbidities								
Diabetes mellitus, n (%)	3.0 (30.0)	12.0 (28.6)	14.0 (19.7)	0.497	11.0 (3.6)	8.0 (18.2)	10.0 (23.3)	0.430
Hypertension, n (%)	10.0 (100)	31.0 (73.8)	55.0 (77.5)	0.195	28.0 (77.8)	35.0 (79.5)	33.0 (76.7)	0.950
Physical activity level								
Physical activity (min/wk)	230 (40.0 – 335)	115 (0.0 – 290)	120 (30.0 – 290)	0.549	150 (35.0 – 290)	137 (1.0 – 310)	120 (40.0 – 290)	0.862
Anthropometric parameters								
Current weight (kg)	70.7 ± 13.8	73.5 ± 15.6	69.1 ± 13.5	0.279	72.6 ± 14.5	70.7 ± 14.5	69.1 ± 13.9	0.566
Height (m)	**1.59 ± 0.92 [a]**	**1.62 ± 0.84 [ab]**	**1.65 ± 0.83 [b]**	**0.034**	**1.60 ± 0.08 [a]**	**1.64 ± 0.09 [ab]**	**1.66 ± 0.07 [b]**	**0.013**
Current BMI (kg/m²)	**28.0 ± 5.4 [a]**	**27.9 ± 5.7 [a]**	**25.2 ± 4.6 [b]**	**0.016**	**28.2 ± 5.9 [a]**	**26.2 ± 4.9 [ab]**	**25.0 ± 4.4 [b]**	**0.018**
Pretransplant weight (kg)	60.7 ± 13.0	62.5 ± 13.6	58.1 ± 11.5	0.203	60.2 ± 13.6	60.2 ± 12.3	59.2 ± 11.8	0.913
Pretransplant BMI (kg/m²)	**24.1 ± 5.8 [a]**	**23.7 ± 4.6 [a]**	**21.7 ± 3.5 [b]**	**0.026**	23.6 ± 5.4	22.5 ± 3.5	21.7 ± 3.6	0.166
Waist circumference (cm)	**105 ± 29.5 [a]**	**98.3 ± 14.5 [ab]**	**91.5 ± 13.4 [b]**	**0.010**	99.8 ± 20.2	94.2 ± 13.4	91.3 ± 13.6	0.056
Calf circumference (cm)	34.9 ± 4.4	34.9 ± 4.2	34.3 ± 3.4	0.687	35.2 ± 4.3	34.6 ± 3.6	33.9 ± 3.6	0.317
Body Composition and Phase Angle								
ASMM (kg)	18.2 ± 3.4	18.9 ± 3.6	19.7 ± 3.3	0.317	18.4 ± 3.3	19.3 ± 3.4	19.9 ± 3.3	0.120
ASMI (kg/m2)	7.1 ± 0 .9	7.1 ± 1.1	7.1 ± 0 .9	0.993	7.1 ± 1.0	7.1 ± 0.9	7.2 ± 0.9	0.930
Fat mass (kg)	**23.1 ± 9.1 [a]**	**22.7 ± 9.1 [ab]**	**20.0 ± 7.2 [b]**	**0.005**	**23.3 ± 9.1 [a]**	**20.0 ± 8.2 [ab]**	**17.2 ±6.7 [b]**	**0.004**
Fat mass (%)	**31.7 ± 10.4 [a]**	**30.2 ± 7.3 [ab]**	**25.4 ± 7.2 [b]**	**0.001**	**31.3 ± 8.1 [a]**	**27.8 ± 7.9 [ab]**	**24.2 ± 6.1 [b]**	**0.001**
PhAº	6.2 ± 0.7	6.4 ± 0.9	6.5 ± 1.0	0.569	6.2 ± 1.1	6.5 ± 0.8	6.6 ± 1.1	0.053
Physical performance and strength								
Handgrip strength (kg)	12.0 (10.0 – 20.0)	15.0 (10.0 – 25.0)	20.0 (12.0 – 28.0)	0.125	**14.0 (4.0 – 62.0)**	**20.0 (4.0 – 40.0)**	**20.0 (4 – 40.0)**	**0.018**
Balance test (score)	4.0 (4.0 – 4.0)	4.0 (3.0 – 4.0)	4.0 (4.0 – 4.0)	0.315	4.0 (3.0 – 4.0)	4.0 (4.0 – 4.0)	4.0 (4.0 – 4.0)	0.286
4-m walking test (m/s)	1.0 ± 0.2	1.1 ± 0.3	1.1 ± 0.3	0.279	1.1 ± 0.2	1.2 ± 0.2	1.1 ± 0.2	0.157
5STS (s)	**15.6 ± 6.7 [a]**	**11.9 ± 2.3 [b]**	**11.5 ± 3.1 [b]**	**0.001**	**13.2 ± 4.8 [a]**	**11.6 ± 2.1 [ab]**	**11.2 ± 2.9 [b]**	**0.034**
SPPB (score)	**10.2 ± 1.4 [a]**	**10.6 ± 1.6 [ab]**	**11.2 ± 1.1 [b]**	**0.016**	**10.4 ± 1.6 [a]**	**11.1 ± 1.3 [b]**	**11.2 ± 1.0 [b]**	**0.009**
Chronic kidney disease data								
Type of dialysis, n (%)								
Peritoneal dialysis	1.0 (10.0)	2.0 (4.8)	4.0 (5.6)	0.779	2.0 (5.6)	3.0 (6.8)	2.0 (4.7)	0.130
Hemodialysis	9.0 (90.0)	35.0 (83.3)	61.0 (85.9)		27.0 (75.0)	39.0 (88.6)	39.0(90.6)	
Peritoneal dialysis and hemodialysis	0.0 (0.0)	5.0 (11.9)	6.0 (8.4)		7.0 (19.4)	2.0 (4.6)	2.0 (4.7)	
Dialysis time (mo)	27.0 (12.0 – 84.0)	48.0 (31.0 – 72.0)	36.0 (24.0 – 72.0)	0.301	48.0 (30.5 – 90.0)	48.0 (26.0 - 72.0)	36.0 (20.0 – 60.0)	0.125
Transplant time (mo)	150 (24.0 – 204)	72.0 (30.0 – 108)	72.0 (42.0 – 132)	0.712	54.0 (24.0 – 150)	81.0 (49.0 – 144)	72.0 (42.0 – 132)	0.235

Number of transplants, n (%)								
1	10.0 (100)	36.0 (85.7)	66.0 (93.0)	0.250	32.0 (88.9)	40.0 (99.9)	40.0 (93.0)	0.813
More than 1 transplant	0.0 (0.0)	6.0 (14.3)	5.0 (7.0)		4.0 (11.1)	4.0 (9.1)	3.0 (7.0)	
Type of donor, n (%)								
Living	5.0 (50.0)	15.0 (35.7)	26.0 (36.6)	0.688	10.0 (27.8)	19.0 (43.2)	17.0 (39.5)	0.344
Deceased	5.0 (50.0)	27.0 (64.3)	45.0 (6.4)		26.0 (72.2)	25.0 (56.8)	26.0 (60.5)	
Drugs								
Tacrolimus (mg/d)	1.0 (0.0 – 8.0)	2.0 (0.0 – 4.0)	2.0 (0.0 – 4.0)	0.774	2.0 (0.0 – 5.0)	0.0 (0.0 – 3.5.0)	2.0 (0.0 – 4.0)	0.299
Cyclosporine (mg/d)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.999	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.929
Azathioprine (mg/d)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.882	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.788
Mycophenolate sodium (mg/d)	0.0 (0.0 – 720)	0.0 (0.0 – 540)	0.0 (0.0 – 720)	0.817	0.0 (0.0 – 720)	0.0 (0.0 – 540)	0.0 (0.0 – 720)	0.523
Mycophenolate mofetil (mg/d)	0.0 (0.0 – 0.0)	0.0 (0.0 –0.0)	0.0 (0.0 – 1000)	0.354	0.0 (0.0 – 0.0)	0.0 (0.0 – 500)	0.0 (0.0 – 1000)	0.341
Everolimus (mg/d)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.831	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.961
Sirolimus (mg/d)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.833	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.966
Prednisone (mg/d)	7.5 (5.0 – 7.5)	5.0 (0.5 – 7.5)	5.0 (0.5 – 7.5)	0.397	5.0 (5.0 – 7.5)	5.0 (5.0 – 7.5)	5.0 (5.0 – 7.5)	0.797
Calcineurin inhibitor use, n (%)	6.0 (60.0)	28.0 (66.7)	45.0 (63.4)	0.901	24.0 (66.7)	26.0 (59.1)	29.0 (67.4)	0.673
Cell proliferation inhibitor use, n (%)	**6.0 (60.0)**	**33.0 (78.6)**	**64.0 (90.1)**	**0.029**	27.0 (75.0)	37.0 (84.1)	39.0 (90.7)	0.169
mTOR inhibitor use, n (%)	3.0 (30.0)	5.0 (11.9)	17.0 (23.9)	0.224	8.0 (22.2)	9.0 (20.4)	8.0 (18.6)	0.924
Corticosteroid drugs, n (%)	10.0 (100)	38.0 (90.5)	64.0 (90.1)	0.585	34.0 (94.4)	41.0 (93.2)	37.0 (86.0)	0.354
Biochemical exams								
Urea (mg/dL)	33.7 (26.7 – 56.7)	49.3 (36.1 – 66.8)	42.8 (34.4 – 55.6)	0.307	46.6 (31.1 – 59.1)	45.3 (38.9 – 62.4)	42.5 (33.6 – 55.6)	0.466
Creatinine (mg/dL)	1.4 (0.8 – 1.8)	1.4 (1.2 – 1.8)	1.4 (1.1 – 1.6)	0.667	1.3 (1.2 – 1.8)	1.4 (1.1 – 1.7)	1.4 (1.1 – 1.7)	0.931
CRP (mg/dL)	0.38 (0.07 – 0.47)	0.39 (0.16 – 1.28)	0.22 (0.07 – 0.59)	0.179	0.52 (0.16 – 0.79)	0.31 (0.15 – 0.59)	0.20 (0.07 – 0.45)	0.146
Kidney function								
GFR (ml/min/1,73m²)	62.3 ± 29.0	52.7 ± 19.3	57.0 ± 20.5	0.351	55.8 ± 21.1	53.6 ± 20.3	58.5 ± 21.3	0.543
Dietary assessment								
Energy (kcal)	**1271 ± 516 [a]**	**1416 ± 421 [a]**	**2000 ± 526 [b]**	**< 0.001**	**1385 ± 473 [a]**	**1702 ± 545 [b]**	**2088± 488 [c]**	**<0.001**
Carbohydrate (g)	**166 ± 80.0 [a]**	**186 ± 65.0 [a]**	**235 ± 80.0 [b]**	**0.001**	190 ± 77.0	221 ± 87.0	226 ± 69.0	0.105
Carbohydrate (%)	**53.1 ± 7.3 [a]**	**52.5 ± 9.2 [a]**	**47.0 ± 8.3 [b]**	**0.003**	**53.8 ± 8.9 [a]**	**51.2 ± 7.7 [b]**	**46.4 ± 7.0 [c]**	**<0.001**
Total protein (g)	**50.6 ± 22.9 [a]**	**61.6 ± 19.5 [a]**	**103.4 ± 34.5 [b]**	**< 0.001**	**54.9 ± 18.2 [a]**	**76.7 ± 20.7 [b]**	**118.9 ± 34.0 [c]**	**<0.001**
Total protein (%)	**15.6 ± 4.6 [a]**	**18.1 ± 4.4 [a]**	**21.4 ± 5.5 [b]**	**<0.001**	**16.2 ± 3.9 [a]**	**19.0 ± 4.4 [b]**	**23.7 ± 5.1 [c]**	**<0.001**
Protein (g/kg)	**0.8 ± 0.4 [a]**	**0.9 ± 0.4 [a]**	**1.6 ± 0.7 [b]**	**<0.001**	**0.8 ± 0.4 [a]**	**1.1 ± 0.4 [b]**	**1.8 ± 0.7 [c]**	**<0.001**
Animal Protein (g)	**30.1 ± 23.6 [a]**	**39.9 ± 17.8 [a]**	**76.3 ± 34.3 [b]**	**<0.001**	**33.1 ± 16.5 [a]**	**52.8 ± 19.3 [b]**	**90.9 ± 34.8 [c]**	**<0.001**
Vegetable Protein (g)	**20.5 ± 9.5 [a]**	**21.7 ± 8.6 [a]**	**27.1 ± 10.1 [b]**	**0.006**	**21.8 ± 10.1 [a]**	**23.9 ± 8.5 [ab]**	**28.0 ± 10.5 [b]**	**0.016**
BCAA (g)	**8.4 ± 4.0 [a]**	**10.5 ± 3.3 [a]**	**17.9 ± 6.2 [b]**	**<0.001**	**9.3 ± 3.2 [a]**	**13.2 ± 3.6 [b]**	**20.7 ± 6.1 [c]**	**<0.001**
Leucine (g)	**3.8 ± 1.9 [a]**	**4.7 ± 1.5 [a]**	**8.0 ± 2.8 [b]**	**<0.001**	**4.2 ± 1.5 [a]**	**6.0 ± 1.6 [b]**	**9.3 ± 2.7 [c]**	**<0.001**
Isoleucine (g)	**2.1 ± 1.0 [a]**	**2.7 ± 0.8 [a]**	**4.6 ± 1.6 [b]**	**<0.001**	**2.4 ± 0.8 [a]**	**3.4 ± 1.0 [b]**	**5.4 ± 1.6 [c]**	**<0.001**
Valine (g)	**2.4 ± 1.1 [a]**	**3.0 ± 0.9 [a]**	**5.2 ± 1.8 [b]**	**<0.001**	**2.7 ± 0.9 [a]**	**3.8 ± 1.0 [b]**	**6.0 ± 1.7 [c]**	**<0.001**
Total fat (g)	**45.8 ± 18.0 [a]**	**46.6 ± 20.0 [a]**	**71.2 ± 25.3 [b]**	**<0.001**	**45.6 ± 20.1 [a]**	**56.7 ± 23.2 [a]**	**77.1 ± 24.8 [b]**	**<0.001**
Total fat (%)	31.3 ± 5.5	29.0 ± 7.4	31.3 ± 6.4	0.229	29.9 ± 7.4	29.3 ± 6.4	32.3 ± 6.3	0.101
Fiber (g)	11.2 ± 6.7	12.4 ± 7.3	14.5 ± 6.3	0.144	12. 5 ± 7.6	12.8 ± 5.6	15.1 ± 6.9	0.157
Misreporting (%)	15.7 ± 5.2	16.4 ± 6.1	16.9 ± 6.1	0.458	16.3 ± 5.4	16.4 ± 5.7	17.3 ± 5.4	0.719

5STS, Five times sit to stand; ASMI, appendicular skeletal muscle index; ASMM, appendicular skeletal muscle mass; BCAA, branched chain amino acids; BMI, body mass index; CRP, C-reactive protein; GFR, glomerular filtration rate; SPPB, Short physical performance battery. Calcineurin inhibitor: tacrolimus or cyclosporine. Cell proliferation inhibitor: azathioprine, mycophenolate sodium, and mycophenolate mofetil. mTOR inhibitors: everolimus and sirolimus.

[abc] Post Hoc de Tukey (p <0,05).

Table 2. Linear regression analysis of number of meals with at least 20 or 30 grams of protein intake and muscle mass, strength and physical performance.

	Model 1			Model 2				Model 3			
All participants (n=123)	**Beta**	**R² (%)**	**p-value**	**Beta**	**R² (%)**	**R² (%)***	**p-value**	**Beta**	**R² (%)**	**R² (%)***	**p-value**
Associations with number of meals containing ≥ 20 g of protein											
Appendicular skeletal muscle mass index (kg/m²)	-0.019	0.04	0.837	-0.056	16.06	0.20	0.600	-0.043	22.08	0.10	0.705
Handgrip strength (kg)	0.129	1.66	0.155	0.035	37.03	2.51	0.716	0.041	37.81	2.76	0.669
Balance test (score)	0.145	2.10	0.110	0.012	12.69	0.01	0.914	-0.009	17.70	0.18	0.929
4-m walking test (m/s)	0.104	1.09	0.251	-0.043	16.80	5.41	0.697	-0.057	21.01	4.76	0.603
5STS (s)	-0.202	4.10	**0.025**	-0.106	22.04	9.64	0.318	-0.233	23.82	6.52	0.269
SPPB (score)	0.205	4.24	**0.022**	0.089	19.14	5.56	0.413	0.079	20.80	4.29	0.474
Associations with number of meals containing ≥ 30 g of protein											
Appendicular skeletal muscle mass index (kg/m²)	0.336	0.11	0.712	0.080	16.23	0.37	0.476	0.129	22.79	0.81	0.129
Handgrip strength (kg)	0.181	3.28	**0.045**	0.094	37.38	2.86	0.377	0.082	38.04	2.99	0.444
Balance test (score)	0.186	3.42	**0.041**	0.055	12.83	0.15	0.660	0.078	17.99	0.47	0.532
4-m walking test (m/s)	0.105	1.12	0.245	-0.001	16.69	5.30	0.993	0.009	20.82	4.57	0.940
5STS (s)	-0.221	4.90	**0.014**	-0.212	23.57	11.17	0.072	-0.204	24.99	7.69	0.088
SPPB (score)	0.258	6,69	**0.004**	0.222	21.09	7.51	0.064	0.229	22.95	6.44	0.061
Participants aged 50 years and over (n= 59)											
Associations with number of meals containing ≥ 20 g of protein											
Appendicular skeletal muscle mass index (kg/m²)	-0.067	0.01	0.612	- 0.124	29.83	0.95	0.414	-0.110	38.83	0.75	0.453
Handgrip strength (kg)	0.134	1.78	0.314	0.071	31.26	2.64	0.649	0.065	35.00	1.80	0.683
Balance test (score)	0.123	1.51	0.353	0.030	15.51	0.06	0.854	0.023	32.59	0.03	0.879
4-m walking test (m/s)	0.020	0.04	0.882	0.012	8.86	0.00	0.943	0.007	25.13	0.01	0.965
5STS (s)	-0.187	3.51	0.155	-0.245	17.68	3.72	0.135	-0.265	21.88	4.27	0.116
SPPB (score)	0.182	1.62	0.167	0.211	10.77	2.77	0.214	0.210	16.52	1.09	0.225
Associations with number of meals containing ≥ 30 g of protein											
Appendicular skeletal muscle mass index (kg/m²)	-0.012	0.02	0.924	0.099	29.34	0.46	0.564	0.114	38.66	0.58	0.510
Handgrip strength (kg)	0.089	0.08	0.501	0.044	31.06	2.44	0.798	0.043	34.85	1.65	0.814
Balance test (score)	0.173	3.00	0.190	0.032	15.50	0.05	0.863	0.044	32.64	0.08	0.808
4-m walking test (m/s)	-0.017	0.03	0.899	-0.081	9.17	0.31	0.677	-0.010	25.13	0.01	0.955
5STS (s)	-0.247	6.13	**0.049**	-0.355	19.90	5.94	**0.047**	-0.446	26.30	8.69	**0.023**
SPPB (score)	0.276	7.65	**0.034**	0.357	13.98	5.98	**0.046**	0.421	21.55	7.72	**0.037**
Participants under 50 years of age (n= 64)											
Associations with number of meals containing ≥ 20 g of protein											
Appendicular skeletal muscle mass index (kg/m²)	0.037	0.01	0.770	-0.050	18.87	0.14	0.754	-0.011	26.61	0.01	0.945
Handgrip strength (kg)	0.107	1.14	0.401	0.066	59.92	0.26	0.553	0.080	61.19	0.35	0.493
Balance test (score)	0.158	2.47	0.215	0.103	13.05	0.62	0.531	0.161	18.78	1.42	0.344
4-m walking test (m/s)	0.180	3.23	0.155	0.042	18.89	0.10	0.792	-0.038	28.74	0.08	0.809
5STS (s)	-0.202	4.09	0.109	-0.105	16.59	0.63	0.518	0.066	62.13	0.24	0.568
SPPB (score)	0.217	4.71	0.085	0.092	17.51	0.50	0.564	-0.032	43.60	0.06	0.823
Associations with number of meals containing ≥ 30 g of protein											
Appendicular skeletal muscle mass index (kg/m²)	0.082	0.06	0.516	-0.002	18.72	0.01	0.990	0.061	26.77	0.17	0.729

Handgrip strength (kg)	0.250	6.26	**0.046**	0.078	59.96	0.30	0.524	0.114	61.43	0.59	0.375
Balance test (score)	0.186	3.47	0.141	0.068	12.65	0.22	0.706	0.037	17.42	0.06	0.812
4-m walking test (m/s)	0.205	4.24	0.103	0.049	18.91	0.12	0.779	0.020	28.68	0.02	0.908
5STS (s)	-0.184	3.39	0.145	-0.107	16.51	0.55	0.545	-0.053	62.02	0.13	0.678
SPPB (score)	0.219	4.80	0.082	0.031	17.06	0.05	0.859	-0.031	43.58	0.04	0.842

Model 1: Crude. **Model 2:** Adjusted for sex, age, waist circumference, energy intake, total protein intake, Glomerular Filtration Rate (GFR) and physical activity .

Model 3: Model 2 and use of immunosuppressive and corticosteroid drugs: calcineurin inhibitor, cell proliferation and mTOR inhibitors, prednisone.

5STS, Five times sit to stand; SPPB, Short physical performance battery.

R^2 (%)*: Is the difference between the R^2 independent variable + adjusts and only R^2 adjusted fixed without variable.

Supplementary Table 1. Pearson correlation analysis between number of meals with at least 20 or 30 grams of protein intake and muscle mass, strength and physical performance.

	Model 1		Model 2		Model 3	
All participants (n=123)	r	p-value	r	p-value	r	p-value
Correlations with number of meals containing ≥ 20 g of protein						
Appendicular skeletal muscle mass index (kg/m²)	-0.02	0.837	0.11	0.245	0.12	0.220
Handgrip strength (kg)	0.13	0.155	0.03	0.716	0.04	0.669
Balance test (score)	0.15	0.109	0.01	0.914	-0.08	0.929
4-m walking test (m/s)	0.10	0.251	-0.04	0.697	-0.05	0.603
5STS (s)	-0.21	**0.025**	-0.09	0.318	-0.10	0.269
SPPB (score)	0.21	**0.022**	0.08	0.413	0.07	0.474
Correlations with number of meals containing ≥ 30 g of protein						
Appendicular skeletal muscle mass index (kg/m²)	0.03	0.712	0.16	0.091	0.15	0.109
Handgrip strength (kg)	0.18	**0.045**	0.08	0.376	0.07	0.444
Balance test (score)	0.18	**0.040**	0.04	0.660	0.06	0.532
4-m walking test (m/s)	0.11	0.245	- 0.08	0.993	0.07	0.939
5STS (s)	-0.22	**0.014**	-0.17	0.071	-0.16	0.088
SPPB (score)	0.26	**0.039**	0.17	0.064	0.18	0.060
Participants aged 50 years and over (n= 59)						
Correlations with number of meals containing ≥ 20 g of protein						
Appendicular skeletal muscle mass index (kg/m²)	-0.07	0.612	0.12	0.414	0.11	0.468
Handgrip strength (kg)	0.13	0.314	0.06	0.649	0.06	0.683
Balance test (score)	0.12	0.353	-0.02	0.939	-0.02	0.901
4-m walking test (m/s)	0.02	0.881	- 0.11	0.450	-0.10	0.511
5STS (s)	-0.19	0.155	-0.20	0.156	-0.21	0.169
SPPB (score)	0.18	0.167	0.11	0.420	0.11	0.436
Correlations with number of meals containing ≥ 30 g of protein						
Appendicular skeletal muscle mass index (kg/m²)	-0.01	0.924	0.21	0.131	0.19	0.183
Handgrip strength (kg)	0.08	0.501	0.04	0.798	0.04	0.814
Balance test (score)	0.17	0.190	0.02	0.935	0.03	0.863
4-m walking test (m/s)	-0.02	0.899	-0.10	0.462	-0.03	0.813
5STS (s)	-0.25	**0.048**	-0.26	**0.044**	-0.32	**0.027**
SPPB (score)	0.28	**0.034**	0.24	**0.047**	0.29	**0.045**
Participants under 50 years of age (n= 64)						
Correlations with number of meals containing ≥ 20 g of protein						
Appendicular skeletal muscle mass index (kg/m²)	0.04	0.770	0.08	0.551	0.05	0.738
Handgrip strength (kg)	0.11	0.401	0.09	0.523	0.10	0.504
Balance test (score)	0.16	0.215	0.11	0.417	0.14	0.302
4-m walking test (m/s)	0.18	0.155	0.07	0.957	-0.04	0.790
5STS (s)	-0.20	0.109	-0,18	0.836	0.09	0.502
SPPB (score)	0.22	0.084	0.04	0.784	-0.03	0.802
Correlations with number of meals containing ≥ 30 g of protein						

	Model 1		Model 2		Model 3	
Appendicular skeletal muscle mass index (kg/m²)	0.08	0.516	0.09	0.490	0.11	0.429
Handgrip strength (kg)	0.25	**0.046**	0.09	0.507	0.12	0.383
Balance test (score)	0.19	0.141	0.07	0.620	0.03	0.812
4-m walking test (m/s)	0.21	0.102	0.19	0.885	0.14	0.919
5STS (s)	-0.18	0.145	-0.05	0.731	-0.05	0.709
SPPB (score)	0.22	0.082	-0.04	0.973	-0.03	0.831

Model 1: Crude. **Model 2:** Adjusted for sex, age, waist circumference, energy intake, total protein intake, Glomerular Filtration Rate (GFR) and physical activity . **Model 3:** Model 2 and use of immunosuppressive and corticosteroid drugs: calcineurin inhibitor, cell proliferation and mTOR inhibitors, prednisone.5STS, Five times sit to stand; SPPB, Short physical performance battery.

5 CONCLUSÕES

De acordo com as análises do Artigo 1, foi possível concluir que a ingestão de ácido graxo ômega-3 e de ácidos graxos poliinsaturados são fatores de proteção para sarcopenia e baixa massa muscular, mas não para força e capacidade funcional, em indivíduos que realizaram transplante renal. Já com as análises do Artigo 2, foi possível concluir que o número de refeições contendo pelo menos 30 gramas de proteína foi inversamente associado ao tempo para realizar o teste de sentar e levantar da cadeira e foi positivamente associado ao escore do SPPB entre indivíduos que realizaram transplante renal com 50 anos ou mais, o que indica que aqueles que consumiram mais refeições com pelo menos 30 gramas de proteína tiveram melhor desempenho nesses dois testes de capacidade funcional. É importante ressaltar que para os mais jovens essa associação não foi observada, mesmo em uma população com alterações metabólicas como os indivíduos que realizaram transplante renal.

6 PERSPECTIVAS

As conclusões encontradas nos dois artigos da presente tese geram perspectivas para a realização de estudos de intervenção dietética no futuro com indivíduos que realizaram transplante renal para verificar o efeito dos nutrientes sobre a sarcopenia e seus componentes (força muscular, massa muscular e capacidade funcional em testes físicos). Ensaios clínicos randomizados deverão avaliar os possíveis efeitos da ingestão de ômega-3 sobre a massa muscular, sarcopenia ou ambas em indivíduos que realizaram transplante renal, bem como se a oferta de refeições com pelo menos 30 gramas de proteína tem um efeito benéfico sobre a massa muscular, o desempenho físico/capacidade funcional e força muscular nesta população. Caso futuros estudos encontrem efeitos benéficos desses nutrientes sobre a sarcopenia e seus componentes em indivíduos que realizaram transplante renal, será possível sugerir novas recomendações nutricionais para esta população a fim de prevenir e ou tratar a sarcopenia e as alterações de seus componentes.

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ANEXOS

ANEXO A - Comprovante de aprovação do projeto de pesquisa pelo Comitê de Ética em Pesquisa (CEP).

UFU — Comitê de Ética em Pesquisa

UNIVERSIDADE FEDERAL DE UBERLÂNDIA/MG

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: AVALIAÇÃO DA PREVALÊNCIA DE SARCOPENIA EM PACIENTES TRANSPLANTADOS RENAIS

Pesquisador: Erick Prado de Oliveira

Área Temática:

Versão: 1

CAAE: 54637716.8.0000.5152

Instituição Proponente: Faculdade de Medicina

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.554.171

Considerações sobre os Termos de apresentação obrigatória:

Todos os termos estão presentes e corretos.

Recomendações:

Não há.

Conclusões ou Pendências e Lista de Inadequações:

De acordo com as atribuições definidas na Resolução CNS 466/12, o CEP manifesta-se pela aprovação do protocolo de pesquisa proposto.

O protocolo não apresenta problemas de ética nas condutas de pesquisa com seres humanos, nos limites da redação e da metodologia apresentadas.

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

UNIVERSIDADE FEDERAL DE
UBERLÂNDIA/MG

PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: AVALIAÇÃO DA PREVALÊNCIA DE SARCOPENIA EM PACIENTES TRANSPLANTADOS RENAIS

Pesquisador: Erick Prado de Oliveira

Área Temática:

Versão: 2

CAAE: 54637716.8.0000.5152

Instituição Proponente: Faculdade de Medicina

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.688.246

Comentários e Considerações sobre a Pesquisa:

Trata-se de emenda para a utilização de novos instrumentos de pesquisa, que foram devidamente justificados.

Considerações sobre os Termos de apresentação obrigatória:

Presentes os novos instrumentos.

Recomendações:

Não há.

Conclusões ou Pendências e Lista de Inadequações:

De acordo com as atribuições definidas na Resolução CNS 466/12, o CEP manifesta-se pela aprovação da emenda proposta.

A emenda não apresenta problemas de ética nas condutas de pesquisa com seres humanos, nos limites da redação e da metodologia apresentadas.

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

ANEXO B – Questionário Internacional de Atividade Física - Forma curta (MATSUDO et al.,2001).

Para responder as questões lembre-se que: Atividades Físicas VIGOROSAS são aquelas que precisam de um grande esforço físico e que fazem respirar MUITO mais forte que o normal.Atividades Físicas MODERADAS são aquelas que precisam de algum esforço físico e que fazem respirar um POUCO mais forte que o normal.

1a. Em quantos dias de uma semana normal você caminha por pelo menos 10 minutos contínuos em casa ou no trabalho, como forma de transporte para ir de um lugar para outro, por lazer, por prazer ou como forma de exercício?

Dias por semana _____   ( ) Nenhum

1b. Nos dias em que você caminha por pelo menos 10 minutos contínuos quanto tempo no total você gasta caminhando por dia?

Horas:_____ Minutos:_____

2a. Em quantos dias de uma semana normal, você realiza atividades MODERADAS por pelo menos 10 minutos contínuos, como por exemplo, pedalar leve na bicicleta, nadar, dançar, fazer ginastica aer6bica leve, jogar vo1ei recreativo, carregar pesos leves, fazer serviços domésticos na casa, no quintal ou no jardim como varrer, aspirar, cuidar do jardim, ou qualquer atividade que faça você suar leve ou aumentem moderadamente sua respiração ou batimentos do coração (POR FAVOR, NAO INCLUA CAMINHADA)

Dias por semana _____   ( ) Nenhum

2b. Nos dias em que você faz essas atividades moderadas por pelo menos 10 minutos contínuos quanta tempo no total você gasta fazendo essas atividades por dia?

Horas:_____ Minutos:_____

3a. Em quantos dias de uma semana normal, você realiza atividades VIGOROSAS por pelo menos 10 minutos contínuos, como por exemplo correr, fazer ginastica aeróbica, jogar futebol, pedalar rápido na bicicleta, jogar basquete, fazer serviços domésticos pesados em casa, no quintal ou no jardim, carregar pesos elevados ou qualquer atividade que faça você suar BASTANTE ou aumentem MUITO sua respiração ou batimentos do coração?

Dias por semana _____   ( ) Nenhum

3b. Nos dias em que você faz essas atividades vigorosas por pelo menos 10 minutos contínuos, quanta tempo no total você gasta fazendo essas atividades por dia?

Horas:_____ Minutos:_____

4a. Estas últimas perguntas são em relação ao tempo que você gasta sentado ao todo no trabalho, em casa, na escola ou faculdade e durante o tempo livre. Isto inclui

o tempo que você gasta sentado no escritório ou estudando, fazendo lição de casa, visitando amigos, lendo e sentado ou deitado assistindo televisão.

Quanto tempo por dia você fica sentado em um dia de semana?

Horas:_____ Minutos:_____

4b. Quanto tempo por dia você fica sentado no final de semana?

Horas:_____ Minutos:_____

APÊNDICES

APÊNDICE A – Termo de consentimento livre e esclarecido

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Você está sendo convidado (a) para participar da pesquisa intitulada "Avaliação da Prevalência de Sarcopenia em Pacientes Renais Transplantados", sob a responsabilidade dos pesquisadores Erick Prado de Oliveira e Aline Silva dos Reis. Nesta pesquisa nós estamos buscando entender a ocorrência de perda de massa muscular e função do músculo (Sarcopenia) após a realização do transplante de rim. O Termo de Consentimento Livre e Esclarecido será obtido pela pesquisadora Aline Silva dos Reis no momento da apresentação do estudo, que será realizado no dia da consulta ambulatorial no Hospital de Clínicas da UFU durante a espera pelo atendimento médico.

Na sua participação você fornecerá informações sobre os seus hábitos alimentares, medidas corporais de peso (obtidos por meio de uma balança), altura (medida por um estadiômetro: instrumento afixado a parede que mede a sua altura) e circunferências do braço, cintura, pescoço e panturrilha (batata da perna) que serão medidas com fita métrica (A fita métrica será colocada em volta destas partes do seu corpo), espessura do músculo adutor do polegar (músculo que fica na sua mão entre os dedos polegar e indicador) medida realizada com um adipômetro, aparelho manual que será encostado levemente na sua mão e a pesquisadora realizará a leitura,também serão medidas as dobras cutâneas (gordura que fica debaixo da pele)com o aparelho adipômetro, sem dor ou desconforto para você. Serão avaliados também os hábitos de ingestão alimentar (o que você geralmente come), qualidade de vida e atividade física através de questionários bastante simples, aplicados pela pesquisadora. Será realizada uma avaliação da sua quantidade de músculo e de gordura corporal (composição corporal), através de um aparelho de ondas magnéticas, onde quatro eletrodos colados na pele (nos pés e nas mãos) fazem a medida (Aparelho chamado de Bioimpedância elétrica), sendo um método simples e rápido, sem dor ou desconforto. Será realizado o teste para verificar a força de preensão manual, ou seja a sua força para apertar objetos (você deverá apertar com toda sua força o aparelho manual chamado dinamômetro, o qual medirá sua força), o teste de caminhada de 4 metros (caminhar por 4 metros como normalmente você caminha),o teste de sentar e levantar da cadeira (sentar e levantar de uma cadeira por 5 vezes) e o teste de equilíbrio estático em pé (em que você de pé, posicionará os seus pés de três formas diferentes e terá que tentar ficar na mesma posição por 10 segundos), ambos são de curta duração, práticos e não exigem grande esforço físico dos avaliados. Todas essas avaliações serão realizadas no dia da sua consulta enquanto você aguarda o atendimento do seu médico. Também será coletada uma amostra do seu sangue no volume total de 10mL (quantidade semelhante a uma colher de chá). Este procedimento pode causar uma leve dor. Entretanto, você já faria este exame de sangue rotineiramente para o seu acompanhamento com o médico.

Em nenhum momento você será identificado. Os resultados da pesquisa serão publicados e ainda assim a sua identidade será preservada.

Você não terá nenhum gasto e ganho financeiro por participar na pesquisa.

Os riscos consistem em seu constrangimento "vergonha" ao ser avaliado tanto durante as avaliações de circunferências/dobras, quanto ao responder os questionários, entretanto este risco será minimizado pelos pesquisadores que adotarão comportamento ético e respeitoso durante tais avaliações. Outro possível risco é o de

identificação dos participantes, de modo a garantir o anonimato dos participantes e minimizar este risco, os avaliados no presente estudo serão codificados para a realização das análises dos dados obtidos, desta forma a identidade dos avaliados será preservada. Os benefícios serão o fornecimento de orientações nutricionais a todos os participantes. Será elaborado material educativo, contendo informações para que os pacientes após o término da participação possam ter noções sobre alimentação saudável.

Você é livre para deixar de participar da pesquisa a qualquer momento sem nenhum prejuízo ou coação.

Uma via original deste Termo de Consentimento Livre e Esclarecido ficará com você. Qualquer dúvida a respeito da pesquisa, você poderá entrar em contato com:

Aline Silva dos Reis. Aluna da Pós-graduação em Ciências da Saúde da Faculdade de Medicina, Universidade Federal de Uberlândia. Endereço: Avenida Pará, 1720- Bloco 2H, Sala 9, *Campus* Umuarama. Fone: 3225-8628.

Erick Prado de Oliveira. Professor Adjunto I, Curso de Nutrição, Faculdade de Medicina, Universidade Federal de Uberlândia. Endereço: Avenida Pará, 1720- Bloco 2U, Sala 20, *Campus* Umuarama. Fone: 3225-8584.

Poderá também entrar em contato com o Comitê de Ética na Pesquisa com Seres-Humanos – Universidade Federal de Uberlândia: Av. João Naves de Ávila, nº 2121, bloco A, sala 224, Campus Santa Mônica – Uberlândia –MG, CEP: 38408-100; fone: 34-32394131

Uberlândia, ... de ....de 201.......

_____
Assinatura dos pesquisadores

Eu aceito participar do projeto citado acima, voluntariamente, após ter sido devidamente esclarecido.

_____
Participante da pesquisa

APÊNDICE B – Instrumento de coleta de dados, Questionário de avaliação.

Questionário Inicial – ANAMNESE

a) Características sócio-demográficas:

Data de Nascimento: ____/_____/_____   Idade (anos): _____

Sexo: ( ) F   ( ) M   Escolaridade: _____

b) Antecedentes Patológicos e Doenças Associadas:

**Pressão Arterial Sistêmica (mm/Hg)_____
(vide prontuário)**

_____
_____
_____
_____

c) Antecedentes Patológicos Familiares:

_____
_____
_____
_____

d) Uso de Medicamentos:

Medicamento	Dose	Posologia

e) Consumo de Cigarros e Bebidas Alcóolicas:

Fuma Atualmente? ( ) Sim   ( ) Não   nº de cigarros/dia_____

Já Fumou Anteriormente? ( ) Sim   ( ) Não

Quanto tempo fumou? _____ Há quanto tempo deixou de fumar? _____

Ingere bebidas alcóolicas atualmente? ( ) Sim   ( ) Não

Tipo de bebida_____

Quantidade_____

Frequência_____

Já Bebeu Anteriormente? ( ) Sim   ( ) Não

Quanto tempo bebeu: _____ Há quanto tempo deixou de beber? _____

f) Informações sobre o Transplante:

Causa da Falência Renal (se conhecida):

_____

Tipo de diálise (antes do transplante): (   ) Hemodiálise   (   ) Diálise Peritoneal

 Tempo de Diálise_____

Peso pré-transplante (kg)_____

1º Transplante? S(   ) N(   ) Tempo de Transplante: _____

Tipo de doador: (   ) Vivo (   ) Cadáver

EXAMES BIOQUÍMICOS

Nome do Exame	Valor do exame do participante	Valor de referência	Data do Exame

Avaliação Antropométrica e de Composição Corporal, Força de Preensão Manual, Capacidade Funcional e Diagnóstico da Sarcopenia

- **Composição Corporal**

Peso pré-transplante (kg)	
Peso atual (kg)	
Estatura (m)	
IMC(kg/m²)	
CC(cm)	
CPant(cm)	
MAP(mm)	
DAS(cm)	

- ✓ **Bioimpedância Elétrica (   )**

- **Força de Preensão Manual**

1º Medida _____ (kg)

2º Medida _____(kg)

3º Medida _____(kg)

Maior Valor das 3 medidas _____ (kg)

- **Capacidade Funcional – SPPB:**

- **Teste de Equilíbrio Estático em pé:**

1ª Posição: Tempo em segundos   _____

2ª Posição: Tempo em segundos   _____
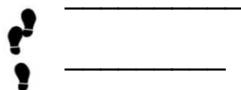
3ª Posição: Tempo em segundos   _____
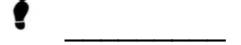
- **Teste de Caminhada de 4 metros (4M GS)**

1ª Tentativa: Caminhada de 4 metros: Tempo de realização do teste _____ segundos = _____m/s

2ª Tentativa: Caminhada de 4 metros: Tempo de realização do teste _____ segundos = _____m/s

- **Teste de Sentar e Levantar da cadeira**

1ª Tentativa: Sentou e levantou 5 x da cadeira em _____

2ª Tentativa: Sentou e levantou 5 x da cadeira em _____

APÊNDICE C – Formulário para aplicação de Recordatório Alimentar 24 horas

Recordatório Alimentar 24 Horas

Código: _____Data Avaliação: ___/___/___

Horário/Refeição	Alimentos/Bebidas/Preparações	Quantidade/ Tipo/Forma de Preparação	Crítica