UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

FACULDADE DE MEDICINA

PROGRAMA DE PÓS GRADUAÇÃO EM CIÊNCIAS MÉDICAS: ENDOCRINOLOGIA

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Preditores de Mortalidade após Alta Hospitalar em Pacientes Idosos com e sem Diabetes melito: Dois anos de seguimento

Porto Alegre, fevereiro de 2019

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Tese apresentada como requisito parcial para a obtenção do título de Doutor em Endocrinologia, à Universidade Federal do Rio Grande do Sul, Programa de Pós-Graduação em Ciências Médicas: Endocrinologia.

Orientador: Prof Dra Ticiana da Costa Rodrigues

Porto Alegre, fevereiro de 2019

FICHA CATALOGRÁFICA

CIP - Catalogação na Publicação

Beretta, Mileni Vanti
Preditores de Mortalidade após Alta Hospitalar em Pacientes Idosos com e sem Diabetes melito: Dois anos de seguimento / Mileni Vanti Beretta. -- 2019.
86 f.
Orientador: Ticiana da Costa Rodrigues.

Tese (Doutorado) -- Universidade Federal do Rio Grande do Sul, Faculdade de Medicina, Programa de Pós-Graduação em Ciências Médicas: Endocrinologia, Porto Alegre, BR-RS, 2019.

1. Envelhecimento . 2. Sarcopenia. 3. Desnutrição. 4. Diabetes Melito. I. da Costa Rodrigues, Ticiana, orient. II. Título.

Elaborada pelo Sistema de Geração Automática de Ficha Catalográfica da UFRGS com os dados fornecidos pelo(a) autor(a).

DEDICATÓRIA

Aos meus pais.

AGRADECIMENTOS

Agradeço imensamente a minha orientadora, Prof. Dra Ticiana da Costa Rodrigues, que me acolheu como aluna de iniciação científica e desde então, acreditou na minha capacidade, sempre me dando oportunidades para aprender e evoluir como futura pesquisadora.

Às alunas de Iniciação Científica, Camila Nery e Juliane V. Feldmam, por todo o interesse e auxílio prestado ao longo das coletas. Aos colegas de grupo de pesquisa, que se tornaram amigos durante estes anos, especialmente ao Fábio F. Dantas Filho e Raquel E. Freiberg que nestes últimos anos colaboraram para que esta etapa se concretizasse. À nutricionista Ciglea C. Nascimento, por todo o carinho e motivação. Aos Profs. e pesquisadores do serviço de Endocrinologia pela oportunidade inicial do meu convívio com a pesquisa e pelo reconhecimento como profissional.

Ao Maikel, por todo o amor e paciência, por ter compreendido a minha ausência e pelo entendimento da minha dedicação à profissão. Aos meus pais Julio e Vera que serviram como idosos modelos em todas as avaliações.

A todos os pacientes que participaram deste projeto, que fizeram com que os dias de trabalho fossem ainda melhores com tantas histórias de vida e que me fizeram ter a certeza de estar no caminho certo.

Esta tese de doutorado segue o formato proposto pelo Programa de Pós-Graduação em Ciências Médicas: Endocrinologia: Faculdade de Medicina, Universidade Federal do Rio Grande do Sul. Será constituída de um referencial teórico e três artigos originais.

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LISTA DE ABREVIATURAS

APM	Adductor pollicis muscle
APMT	Adductor pollicis muscle thickness
BMI	Body mass índex
CC	Calf Circumference
CDC	Center for Disease Control and Prevention
CI	Charlson Comorbity Index
CNPQ	Conselho Nacional de Desenvolvimento Científico e Tecnológico
DCNT	Doenças crônicas não transmissíveis
ER	Emergency room
FAM	Força do aperto de mão
GLIM	Global Leadership Initiative on Malnutrition
GLM	General linear model
HAS	Hipertensão artérial sistêmica
HR	Hazard ratio
HS	Handgrip strength
IADL	Instrumental Activities of Daily Living
IQR	Interquartile range
ISAK	International Society for the Advancement of Kinathropometry
LOS	Lenght of hospital stay
MNA	Mini Nutritional Assessment
OMS	Organização Mundial da Saúde
SAH	Systemic arterial hypertension

T2D	Type 2 diabetes
TUG	Timed Up and Go test
WL	Weight loss

RESUMO

A perda de massa muscular e a desnutrição durante a hospitalização são fatores que contribuem para a pior qualidade de vida, morbidade e mortalidade no paciente idoso. O objetivo deste trabalho foi identificar os preditores de mortalidade após a alta hospitalar. Foi realizado um estudo de coorte prospectivo, com seguimento de dois anos, no Hospital de Clínicas de Porto Alegre (HCPA), no período de julho de 2015 a dezembro de 2016. Foram incluídos pacientes acima de 60 anos, com até 48 horas de admissão hospitalar, que concordassem em participar da pesquisa e assinassem o termo de consentimento. Foram excluídos pacientes que não deambulavam, aqueles com alguma amputação, demência ou sequela motora avançada, aqueles com passagem pelo centro de terapia intensiva e aqueles com permanência hospitalar menor que dois dias. A avaliação nutricional foi realizada através da Mini Avaliação Nutricional (MAN). A presença de sarcopenia foi avaliada pelo teste de mobilidade "*time up and Go*" (TUG), pela força do aperto de mão (FAM) através de um dinamômetro analógico (Saehan) e pela circunferência da panturrilha (CP). A presença de sarcopenia foi considerada quando: TUG<0,8m/s, FAM <20Kg para mulheres e <30Kg para homens e CP<34 cm para homens e <33 cm para mulheres. A espessura do músculo adutor do polegar (MAP) foi avaliada na mão dominante utilizando um plicômetro (Lange), os valores obtidos foram divididos em quartis. O nível de independência foi avaliado pelo questionário de atividades instrumentais da vida diária (AIVD). Variáveis como peso, CP, FAM, MAP foram avaliadas na admissão e na alta hospitalar. O prontuário do paciente foi consultado para completar dados sobre o histórico de saúde, para a pontuação do questionário de risco de quedas e avaliação de quedas durante a internação. Após a alta hospitalar, os pacientes tiveram seu prontuário consultado e também foram contatados por telefone em: 1,3,6,9,12 e 24 meses. Nestes contados, os dados verificados foram: o estado geral de saúde, ocorrência de internação em outra instituição, perda ou ganho de peso após alta hospitalar e quedas. A

mortalidade foi investigada por consulta ao prontuário, contato telefônico e registro do óbito. Foram incluídos 616 pacientes, dos quais seis pacientes desistiram de participar após a alta hospitalar. Os 610 pacientes analizados, tinham idade média de 71,35 ± 6,45, 51% do sexo feminino, 77% de cor branca e 90% sedentários. Cerca de 15% eram fumantes e 77% possuiam o 1º grau concluído. Os pacientes foram estratificados de acordo com a presença de diabetes melito tipo 2 (DM2), mortalidade (sim e não) e tempo de internação (acima e abaixo de 7 dias). O DM2 estava presente em 50,6% da coorte, hipertensão arterial em 70% e neoplasia de qualquer natureza em 27,8%. No período de dois anos, 170 (28%) dos pacientes foram a óbito e 234 (40%) reinternaram. As causas dos óbitos foram: 47 (7,6%) por doença cardiovascular, 57 (9,3%) por neoplasias, 39 (6,3%) por choque séptico, 13 (2%) por doenças pulmonares e 15 (2,3%) por outras causas. A sarcopenia estava presente em 237 (39%) dos pacientes já na admissão hospitalar**.** Quando comparados ao pacientes sem DM2, os pacientes com DM2 apresentaram mais quedas intra hospitalar (34% vs. 19%, p=0,001), bem como maior risco de quedas (40 pontos vs. 35, p=0,006), mais sobrepeso (54,5% vs. 38%, p=0,005), menor FAM (19,62±7,5 vs. 21.,19±7,3, p=0,009), menor mobilidade (0,54 vc. 0,60, p<0.001) e maior prevalência de sarcopenia (46,5% vs. 31%, p=0,001). Análises ajustadas de regressão de Cox mostraram como preditores de maior tempo de internação: redução da FAM durante a hospitalização, perda de >5% do peso corporal e presença de desnutrição. Os preditores de mortalidade foram: tempo de internação acima de 7 dias, presença de DM2, qualquer tipo de neoplasia, menor espessura do MAP, maior nível de dependência e a coexistência de DM2 e sarcopenia. Este estudo mostrou que os pacientes idosos apresentam desfechos desfavoráveis em função da sua condição de base, mas também pelo processo de desnutrição e perda de força pela própria internação hospitalar. Identificamos também que a avaliação da espessura do MAP pode ser uma ferramenta de fácil aplicação na prática clínica com grande potencial

para identificar os pacientes em maior risco de piores desfechos nutricionais e clínicos, incluindo mortalidade.

Palavras-chave: idosos, sarcopenia, desnutrição, diabetes melito, mortalidade

ABSTRACT

Loss of muscle mass and malnutrition during hospitalization are factors that contribute to poor quality of life, morbidity and mortality in the older patient. The objective of this study was to identify possible predictors of mortality after hospital discharge. A prospective cohort study with a two-year follow-up was carried out at the Hospital das Clinicas de Porto Alegre (HCPA) from July 2015 to December 2016. Patients older than 60 years, with up to 48 hours of admission hospital, who agreed to participate in the study and to sign the consent form. Were excluded patients, those with any amputation, dementia or advanced motor sequelae, those with an intensive care unit and those with a hospital stay of less than two days. The nutritional screening was evaluated through the Mini Nutritional Assessment (MNA). The presence of sarcopenia was evaluated by the Timed Up and Go test"(TUG)", by handgrip strength (HS) through an analog dynamometer (Saehan) and by calf circumference (CC). The presence of sarcopenia was considered when TUG <0.8m / s, HS <20Kg for women and <30Kg for men and CC <34cm for men and <33cm for women. The adductor pollicis muscle thickness (APMT) was evaluated in the dominante hand using a plicometer (Lange), the values were divided into quartiles. The level of autonomy was validated by the Instrumental Activities of Daily Living (IADL). Variables such as weight, CC, HS, APMT were evaluated at admission and at hospital discharge. The medical records were consulted to verify data on the health history, risk of falls (Morse questionario) and falls during hospitalization. After hospital discharge, the patients had their medical records consulted and were also contacted by telephone at: 1,3,6,9,12 and 24 months after hospital discharge. The data verified were: general health status, the occurrence of hospitalization in another institution, weight gain or hospital discharge and falls. Mortality was investigated by consulting the medical record, telephone contact and death register. A total of 610 patients were included, with a mean age of 71.35 ± 6.45, 51% women, 77% white and 90% sedentary. About 15% were smokers and

77% had completed 1st grade. Patients were stratified according to the presence of type 2 diabetes (T2D), mortality (yes and no) and length of stay (above and below 7 days). T2D was present in 50.6% of the cohort, arterial hypertension in 70% and neoplasia of any nature in 27.8%. In the two-year period, 170 (28%) of the patients died and 234 (40%) were rehospitalization. The causes of death were: 47 (7.6%) from cardiovascular disease, 57 (9.3%) from neoplasias, 39 (6.3%) from septic shock, 13 (2%) from pulmonary diseases, and 15, 3%) for other reasons. Sarcopenia was present in 237 (39%) patients at hospital admission. When compared to patients without T2D, patients with T2D had more in-hospital falls (34% vs. 19%, p = 0.001), as well as an increased risk of falls (40 points vs. 35, p = 0.006), and overweight (54.5% vs. 38%, p = 0.005), lower HS (19.62 ± 7.5 vs. 21. 19 ± 7.3, p = 0.009), lower mobility (0.54 v / 60, p <0.001) and a higher prevalence of sarcopenia (46.5% vs. 31%, p = 0.001). Cox regression analysis showed that the predictors of longer hospitalization were: Low HS during hospitalization, loss of> 5% of body weight and presence of malnutrition. The predictors of mortality were: time of hospitalization longer than 7 days, presence of T2D, any type of neoplasia, lower APMT, higher level of dependence and coexistence of TD2 and sarcopenia. This study showed that older patients present unfavorable outcomes due to their underlying condition, but also due to malnutrition and loss of strength due to hospitalization. We also identified that APMT assessment may be a tool easily applied in clinical practice with great potential to identify patients at greater risk of worse nutritional and clinical outcomes, including mortality.

Keywords: older people, sarcopenia, malnutrition, type 2 diabetes, mortality

REFERENCIAL TEÓRICO

Envelhecimento Populacional

No Brasil a transição demográfica trouxe alterações relevantes nos indicadores de morbidade e mortalidade [1]. Transição que tem como característica uma sequência de eventos que resultam em baixas taxas de mortalidade e de fecundidade, crescimento negativo como por exemplo: redução dos nascimentos e elevada proporção do número de idosos[1]. A queda da mortalidade dos idosos pode ser explicado por diversos fatores, como: melhores condições de vida, aos avanços na medicina que proporcionaram melhor controle, tratamento e prevenção de doenças crônicas não transmissíveis (DCNT) como a hipertensão arterial sistêmica (HAS) e o diabetes melito tipo 2 (DM2)[1], bem como diagnóstico precoce de diversas condições clinicas.

Segundo dados demográficos do Instituto Brasileiro de Geografia e Estatística (IBGE), no período de 5 anos, compreendido entre 2012 a 2017, houve um crescimento de 18% da população na faixa etária idosa, correspondendo a 4,8 milhões de novos idosos. As mulheres são maioria expressiva nesse grupo, com 16,9 milhões (56%), enquanto os homens são 13,3 milhões (44% do grupo)[2]. Estima-se um crescimento ainda maior da população idosa nos próximos anos, devendo atingir 22% da população geral em 2050, cerca de 2 bilhões de habitantes[3]. Concomitante ao crescimento do número de idosos e em paralelo ao aumento da expectativa de vida percebe-se o adoecimento e a suscetibilidade a eventos adversos, bem como complicações clínicas podendo aumentar o número de internações hospitalares.

Problemas associados ao envelhecimento

O processo natural de envelhecimento, ou Senescência, não traz qualquer problema à saúde[4]. Por outro lado, o envelhecimento patológico, ou senilidade, ocorre concomitante ao processo de envelhecimento, porém com danos que levam a deficiências funcionais, alterações cognitivas, musculares e associado à DCNT como obesidade, HAS e DM2.

1. Sarcopenia

A sarcopenia é definida pela perda progressiva e generalizada de massa muscular esquelética e força muscular resultando em risco aumentado para desfechos adversos como declínio funcional, quedas, baixa qualidade de vida e aumento da mortalidade[5,6,7]. Pode ser atribuída ao próprio processo de envelhecimento, chamada de sarcopenia primária ou associada à idade; mas também pode ser secundária e estar relacionada a outras causas como: processos inflamatórios, doença sistêmica, inatividade física por estilo de vida sedentário, imobilidade ou deficiência[8]**.** Além disso, a ingestão inadequada de alimento, que pode ser devido à anorexia, má absorção, acesso limitado a alimentos saudáveis ou capacidade limitada para se alimentar[9] incluindo as dificuldades de mastigação e de deglutição podem contribuir para o desenvolvimento da sarcopenia.

Para diagnosticar a sarcopenia, o Grupo Europeu de Trabalho em Sarcopenia em Idosos (*European Working Group on Sarcopenia in Older People*)[10] recomenda avaliar a presença de baixa massa muscular, baixa função muscular (força ou desempenho) de acordo com o proposto pelo algoritmo (Anexo I). Em recente revisão da diretriz, a força muscular passou a ser considerada melhor do que a massa muscular como prognóstico de piores desfechos[11,12,13] (Anexo II). Assim, a força muscular é o primeiro critério avaliado e a baixa força muscular caracteriza-se como “provável sarcopenia”; o segundo critério da nova diretriz avalia se existe baixa qualidade ou quantidade muscular; e o terceiro critério avalia a baixa performance, sendo a presença dos três critérios classificada como sarcopenia severa[9].

A atualização da diretriz propõe como primeiro passo, a inclusão do questionário SARC-F[14]como uma ferramenta de triagem; a força muscular é avaliada pela força do aperto de mão utilizando um dinamômetro[15]. A baixa massa muscular é avaliada através de métodos como tomografia computadorizada, bioimpedância e ressonância magnética; a antropometria realizada através da medida da circunferência da panturrilha (CP) pode ser feita quando não há outros métodos diagnósticos disponíveis[9]. Neste sentido, um estudo realizado em Pelotas/RS definiu os pontos de corte para a CP, nos quais : ≤34 cm (homens) e ≤33 cm (mulheres)[16]. Por fim, a baixa performance pode ser avaliada pelo teste de caminhada como *Timed get-up-and-go test* [17].

A prevalência de sarcopenia tem um aumento linear com a idade [5], sendo de 6% a 22% no indivíduo acima de 65 anos, podendo variar de acordo com a região[18]. No ano de 2016 a Organização Mundial de saúde (OMS) incluiu a sarcopenia na Classificação estatística Internacional de doenças e problemas de saúde relacionados (*International Statistical Classification of Diseases and Related Health Problems -ICD*). A classificação como doença ocasionou um aumento expressivo de publicações, que incluem estudos de mecanismos de rastreio, diagnóstico e manejo, bem como a publicação da primeira diretriz em 2018[19].

A importância de avaliar a perda de massa muscular no paciente idoso no contexto hospitalar foi descrita recentemente como um dos critérios diagnósticos para avaliar a desnutrição na diretriz *Global Leadership Initiative on Malnutrition* (GLIM)[20]. De acordo com o GLIM, não há consenso sobre a melhor forma de medir e definir a massa muscular em contextos clínicos, portanto, a recomendação é avaliar por métodos como: absorciometria de dupla energia, bioimpedância, ultra-som, tomografia computadorizada ou ressonância magnética, e como medidas alternativas, na falta dos equipamentos, recomenda-se o exame físico ou medidas antropométricas como circunferência muscular do braço ou CP.

2. Desnutrição

As alterações fisiológicas que acompanham o envelhecimento, como as modificações no paladar e olfato, perda da dentição, poli farmácia, viver sozinho entre outros fatores socioeconômicos contribuem para a baixa ingestão alimentar[21]. A desnutrição é definida como o estado resultante da deficiência de nutrientes que podem causar alterações na composição corporal, na funcionalidade e estado mental com pior prognóstico clínico[21], tal condição é frequentemente encontrada no ambiente hospitalar[21-22]. Apesar de piorar o quadro de saúde dos indivíduos, muitas vezes é negligenciada no ambiente hospitalar[22] e pode apresentar como principais complicações: pior resposta imunológica, atraso no processo de cicatrização, risco elevado de complicações cirúrgicas e infecciosas, maior probabilidade de desenvolvimento de lesões por pressão, aumento no tempo de internação, do risco de mortalidade, e consequentemente aumento dos custos hospitalares[23].

A prevalência de desnutrição é entre 20 e 50% em adultos hospitalizados, podendo variar de 40 a 60% no momento da admissão do paciente, sendo ainda pior no paciente crítico e nos idosos[23]. O paciente idoso apresenta maior propensão à desnutrição, demanda de maior tempo de permanência hospitalar, com consequente piora do estado nutricional, o que pode levar a um aumento das taxas de mortalidade[24].

Apesar da elevada prevalência de desnutrição hospitalar e consequente desfechos negativos, os profissionais de saúde ainda estão pouco sensibilizados para o rastreio nutricional. Os problemas relacionados ao estado nutricional, causadores de risco clínico, não são muitas vezes identificados, enquanto outras características da doença primária dos pacientes são rastreadas e tratadas rotineiramente como a desidratação, a febre e a hipertensão arterial[25]. Diante deste quadro, que se prolonga por décadas, uma campanha intitulada "*Diga não à desnutrição*" foi lançada em 2018 com o objetivo de reduzir as taxas de desnutrição hospitalar por meio de uma série de ações que incluem triagem, diagnóstico, manejo e tratamento da desnutrição[22].

No paciente idoso a avaliação nutricional no ambiente hospitalar pode ser realizada pela Mini avaliação nutricional (MAN). É um instrumento validado e avalia o risco nutricional ou a desnutrição já instalada. O questionário da MAN é constituído por questões que avaliam a ingestão alimentar e a perda ponderal nos últimos três meses, mobilidade, ocorrência de estresse psicológico ou doença aguda recente, medidas antropométricas, como: circunferências de braço e panturrilha; o número de refeições consumidas, ingestão de líquidos e de alimentos; autonomia para se alimentar; avaliação global, com perguntas relacionadas ao estilo de vida e medicamentos utilizados e uma autoavaliação relativa à saúde e nutrição do idoso[26]. Baixos escores da MAN pode predizer tempo de hospitalização e aumento do risco de mortalidade[27].

3. Diabetes Melito

Segundo dados do *Center for Disease Control and Prevention* (CDC), aproximadamente um quarto das pessoas com mais de 65 anos tem diabetes e estima-se que essa proporção aumente rapidamente nas próximas décadas[28]. A presença de DM2 nesta faixa etária, cursa com acelerado declínio da massa muscular, redução da capacidade funcional, gerando maior dependência e risco de institucionalização, bem como, aumento da taxa de mortalidade[29]. Dados do DATASUS de 2016 apontam que no Rio Grande do Sul houveram 3.385 óbitos por DM2 na população acima de 60 anos, e no município de Porto Alegre houveram 630 óbitos por DM2 neste mesmo ano[30].

Com relação à mortalidade, o Brasil registrou crescimento de 12% do número de mortes por DM2, de 2010 a 2016 (Ministério da Saúde). Estudo prospectivo com 8 anos de seguimento[31] avaliou clinicamente um grupo de pacientes com DM2 durante sua internação hospitalar e os acompanhou durante um período pós-alta hospitalar com o objetivo de identificar fatores prognósticos de mortalidade nestes pacientes. Os fatores preditores de morte foram idade acima de 65 anos na internação hospitalar, hipertensão arterial há mais de 5 anos, taxa de filtração glomerular abaixo de 60 ml/min e excreção urinária de proteína acima de 300mg/24h, foi observado que a mortalidade em pacientes com DM2 foi 3 vezes maior em comparação aos pacientes sem DM2[31].

4. DM2 e sarcopenia no paciente idoso

A presença de sarcopenia parece ter uma relação independente do DM2[32,33]. O músculo esquelético requer a presença de insulina para a captação da glicose na periferia dos tecidos, a glicose será utilizada como fonte de energia ou será armazenada sob a forma de glicogênio. A redução da massa muscular esquelética devido à sarcopenia altera o metabolismo da glicose pela insulina, levando a resistência à ação da insulina, tornando a sarcopenia um fator que contribui para o início ou piora do diabetes[32-34].

Pacientes idosos com DM2 apresentam menor massa muscular e força em relação aos idosos sem DM2 de mesma idade[35]. Portanto, identificar precocemente e tratar a sarcopenia pode desempenhar um papel importante no tratamento global do diabetes em pacientes idosos afetados por ambas as doenças[36].Além disso, a presença de sarcopenia no paciente com DM2 parece contribuir para outras complicações relacionadas ao DM; a força muscular reduzida, avaliada pela FAM, está associada com nefropatia diabética, maior ocorrência de eventos cardiovasculares, de hospitalizações e de mortalidade[37] . Da mesma forma, a presença de retinopatia não proliferativa foi associada significativamente à sarcopenia e a retinopatia proliferativa contribuiu para baixa qualidade muscular[36] e pior prognóstico para pacientes com pé diabético, com maior frequência de úlceras nos pés e maior porcentagem de amputação em comparação aos pacientes com DM2 sem sarcopenia[38].

5.Internações Hospitalares

A internação hospitalar é um importante recurso no cuidado ao paciente idoso, porém quando repetidas e prolongadas, podem produzir consequências negativas à saúde destes pacientes[39,40]. No município de Porto Alegre no ano de 2012 houveram 716.730 internações hospitalares[30]. No Hospital de Clínicas de Porto Alegre (HCPA), no período de julho de 2015 a dezembro de 2017 houveram 12.906 admissões de pacientes acima de 60 anos, incluindo internações em UTI, cirurgias e procedimentos eletivos (dados da autora).

As internações nesta faixa etária são frequentes, segundo dados do *Brazilian Longitudinal Study of Aging* (ELSI)[40], os 9.389 idosos participantes, 10,2% já haviam sido hospitalizados nos 12 meses anteriores ao estudo e no período de um ano de seguimento 11,6% tiveram pelo menos uma hospitalização[40]. Embora seja necessária em situações de doença aguda ou crônica agudizada, pode resultar em uma série de complicações não relacionadas ao motivo inicial da internação[41]. Essas complicações podem elevar os dias de hospitalização e consequentemente ocasionar um declínio funcional, intervenções cirúrgicas não programadas, bem como maior morbidade e mortalidade[41,42].

Outro fator importante durante a hospitalização é a inatividade física do paciente idoso, a qual contribui claramente para uma série de resultados negativos, como: redução na capacidade de realizar atividades da vida diária, alteração da composição corporal com prejuízo da massa muscular, maior incidência de readmissão e institucionalização[4243]. Com relação a alteração da composição corporal e força muscular; idosos hospitalizados, pelo menos 8 dias ao ano, apresentam menor força muscular e massa muscular quando comparados com idosos não hospitalizados[44].

De fato, o paciente idoso hospitalizado apresenta maior risco de desnutrição, sarcopenia e consequentemente maior tempo de hospitalização e mortalidade.

6. Preditores de Mortalidade no paciente idoso

Muitos pacientes idosos após uma hospitalização cursam com um declínio físico progressivo e significativo resultando em altas taxas de mortalidade nos anos seguintes[45]. A identificação dos possíveis preditores de mortalidade durante a hospitalização ou mesmo após a alta hospitalar seria de grande ajuda para o cuidado.

Preditores de mortalidade em pacientes idosos podem ser úteis por várias razões, tais como: identificar grupos de maior risco de desfechos desfavoráveis, ter outras opções de tratamento, bem como aconselhar o paciente e familiares[45]. Estudos prévios identificaram que o status funcional na admissão, o nível de dependência, a baixa FAM, sexo masculino, presença de neoplasias, tempo de internação, úlcera de pressão, insuficiência cardíaca e índice de massa corporal[31], creatinina >3mg/dl, bem como o baixo nível de albumina sérica foram associados à mortalidade em 12 meses [31,45,46]. Em um estudo prospectivo de 8 anos de seguimento constatou-se que os preditores de mortalidade para pacientes com DM2 foram os fatores sociodemográficos, incluindo idade mais avançada, sexo masculino, cor branca, menor renda, e tabagismo[31]. Além disso, pacientes com neoplasia, a idade >80 anos, a presença de desnutrição, o tamanho do tumor e a menor mobilidade foram considerados preditores de 1 ano de mortalidade[46].

Predizer os fatores associados à mortalidade no paciente idoso é necessário, incluindo também fatores relacionados ao estado nutricional e à sarcopenia.

JUSTIFICATIVA

As pessoas estão vivendo mais e convivendo mais tempo com doenças crônicas e condições incapacitantes. Uma vez hospitalizado, o idoso pode desenvolver uma série de problemas, muitas vezes não relacionados ao motivo principal da sua hospitalização. É possível perceber que a desnutrição, a sarcopenia e o diabetes melito podem estar presentes no envelhecimento, de maneira isolada ou combinada, mas contribuindo para desfechos negativos, especialmente quando o idoso é hospitalizado.

Objetivamos investigar os fatores associados a desnutrição, sarcopenia e DM2 durante o período da hospitalização e a associação com a mortalidade após a alta hospitalar.

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CAPÍTULO II

"Predictors of length of hospital stay and mortality in a cohort of older people"

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Abstract

Background: Prolonged hospitalization can affect the health of older people and, when hospitalized for more than seven days, causes a worsening of nutritional status and a predisposition to fragility. The aim of the study was to evaluate whether weight loss (WL) during hospitalization and a reduction of handgrip strength (HS) are predictors of hospitalization time and mortality after hospital discharge in older people. **Methods:** This was a prospective cohort study carried out with older patients admitted to a public hospital, with the approval of the local Ethics Committee. Patients from different sectors of the hospital were recruited from July 2015 to December 2016 within 48 hours of admission. The HS was evaluated with an analog dynamometer according to a standardized protocol. Patients were stratified according to the length of hospital stay of less than or equal to seven days. **Results:** We included 610 patients, with an average age of 71.35 ± 6.45; of these, 51% patients were female and 77% were Caucasian, with a length of hospital stay of 14 (5–120) days. Among those who remained hospitalized for more than seven days, 88.2% were sedentary, 50.3% were diabetic, 72.8% were hypertensive, and 49.1% presented neoplasia. In addition, 43.2% showed a loss of muscle strength, and during hospitalization their weight reduced by an average of 1.45 kg (vs. 0.48 kg, $p < 0.001$). Overall mortality was 27.4% in the two-year period and 30.3% among those hospitalized for more than seven days ($p=0.032$). After adjusting for gender, age and neoplasia, being hospitalized for longer than seven days, having type 2 diabetes and being malnourished were factors associated with an increased risk of death (HR: 1.75, $p = 0.02$, HR = 1.45, $p = 0.03$, HR: 1.28, $p = 0.019$, respectively). **Conclusions:** We conclude that older people who lost more weight during hospitalization and who showed reduced HS remained hospitalized longer. Our study demonstrated that length of stay and nutritional status of older patients, as well as having diabetes, are important risk factors for mortality.

Keywords: length of hospital stay; handgrip strength; mortality; older people; malnutrition.

Introduction

Hospital admission is an important part of care for older patients, but hospitalizations, when recurrent and prolonged, can have negative consequences on the health of these individuals[1,2]. The hospitalization of the older patients is related to decreased functional capacity and quality of life, as well as complications unrelated to the reason for hospitalization[2-4]. The prevalence of malnutrition among the older patients at admission varies from 20–50% and may increase during hospitalization, resulting in worse clinical outcomes, an increased risk of general mortality and increased hospital readmission rates[5-8]. In fact, many studies have shown that adult or older patients who are hospitalized for more than seven days present a worsening nutritional status[6,9,10], with unintentional weight loss (WL), muscle atrophy and loss of muscle strength. Muscle strength in older patients can be assessed by the handgrip strength (HS) of the dominant hand, since evidence suggests[11,12] that HS has predictive validity for a decline in cognition, mobility, and increased mortality in the older patients. There are positive correlation among needed of hospitalization and increased mortality rate and morbidity, worsening the prognosis and predisposition to the fragility syndrome[3,4]. Based on these factors, we aimed to evaluate whether unintentional WL during hospitalization and the reduction of HS are predictors of hospitalization time and mortality after hospital discharge in a sample of older patients, as well as the identification of other factors associated with length of hospital stay and mortality.

Methods

In the period from July 2015 to December 2016, all hospitalized patients with more than 60 years from internal medicine unite and specialties were screened. Were included patients with up to 48 hours of hospital admission, who agreed to participate in the study and signed the consent form. Were excluded patients who did not deambulate, those with any amputation, mental decline or advanced motor sequalae; those who were treated at the Intensive Care Unit, and those who were in hospital for less than two days. The study was conducted in accordance with the principles established by the Declaration of Helsinki with the approval of the local Institutional Ethics Committee

All evaluations were performed within 48 hours of admission to the ward and data on gender, age, main diagnosis, number of comorbidities (excluding malnutrition) and nutritional parameters were collected through standard questionnaires and patient records. To evaluate the independence level, the Instrumental Activities of Daily Living (IADL)[l4] was performed. The IADL scale assesses eight tasks, providing information about functional skills that are necessary to live independently in the community. Each activity can be scored as either 1 (can perform task independently) or 0 (not able to do), with a score ranging from 0 (low function, dependent) to 8 (high function, independent)[14].

Nutritional status was evaluated through the Mini Nutritional Assessment (MNA), using the following reference values: normal nutritional status (≥24 to 30 points), risk of malnutrition (≤17 to 23.5 points) and malnutrition (<17 points)[15]. In order to evaluate the percentage of unintentional WL during the hospitalization period.

The HS was evaluated using an analog dynamometer (Saehan®) in the dominant hand and in three measurements with an interval of one minute between them. The patient was instructed to sit with their arm flexed at a 90° angle and exert a constant force for 10 seconds.

HS, as well as body weight, was evaluated in two moments: at admission and at hospital discharge. The cut-off points used were those proposed by Laurentani et al.[16], which defined muscle weakness as <20kgf for women and <30kgf for men. The HS test was applied in two moments: within the first 48 hours of admission and at discharge.

The sample calculation was based on previous study[13] we would need 518 patients, 259 with T2D and 259 without T2D. We increased the sample to 610 patients, predicting a possible loss of follow-up of around 15%. This study showed that there were 93 deaths per year after hospitalization, and patients with T2D had a 3-fold higher mortality than those without T2D. The estimated power was 90% with an alpha error of 5%, $p < 0.05$.

Outcomes

Overall all-cause mortality within two years follow-up after hospital discharge were considered the primary endpoint, confirmed by death certificate, by contact with the relative or by medical records in the case of death at an institution. The secondary endpoint included the length of hospital stay (LOS), which was considered from the date of hospital admission until the discharge date. Most of the patients had a passage through the emergency department of the hospital before being referred to a ward, so we evaluated the different days in each part of the hospital. After discharge, all patients were followed up by telephone contact and by appointment to the medical chart after 30 days and every three months up to 24 months.

Statistical analysis

The patients were stratified according to LOS, using seven days as a cut-off point (LOS ≤7 and LOS >7). All quantitative variables were tested for normality (Kolmogorov-Smirnov test). We performed the chi-square test for qualitative variables, the independent t-test for parametric quantitative variables and the Mann-Whitney test for non-parametric variables. The paired t-test was performed with anthropometric variables collected within 48 hours of admission and discharge. The effect size was calculated using the formula proposed by Rosenthal et al.[17].

We performed a univariate analysis (GLM) of LOS >7 days as a dependent variable and each covariate separately. For multivariate analysis, we considered $p<0.20$; adjustment covariates were age, sex, the presence of neoplasia, the presence of type 2 diabetes (T2D) and IADL scale.

Kaplan-Meier analysis was stratified by gender to assess survival according to LOS and nutritional status. Cox analysis was performed to assess general mortality and length of hospital stay with adjustments for age, gender and the presence of neoplasia. To analyze the loss of HS during the hospitalization period, we considered the percentage loss quartile, with a loss ≤ 5% showing the first quartile, >5% to ≤ 10% indicating the second quartile, >10% to ≤20% indicating the third quartile and ≥20% indicating the last quartile. To evaluate the percentage of loss of HS during hospitalization, we considered how much loss occurred in relation to the baseline value.

Results

Of the 616 patients included in the study, six discontinued from participating in the study after discharge. We analyzed 610 patients, with a mean age of 71.35 ± 6.45, with 51% being female and 77% Caucasian. The general characteristics of the patients were stratified according to the length of hospitalization LOS ≤7 or >7 days (**Table 1**). Among the patients who remained hospitalized for more than seven days, 88.2% were sedentary, 50.3% had T2D, 72.8% had hypertension and 49.1% had some form of neoplasia. In addition, 43.2% showed a loss of muscle strength and were more dependent, as identified through the IADL scale (5 ±

1.8 vs. 7 ± 1.6, p <0.001), when compared to patients who remained hospitalized with LOS ≤7.

Regarding nutritional status, 27% of patients with LOS>7 days were malnourished at the time of admission (vs. 14% LOS ≤7 days, p=0.03). **Table 2** shows the differences in HS and body weight during hospitalization, stratified according to LOS. A reduction in body weight of 1.45 kg was observed among patients who remained hospitalized for more than seven days (P = 0.08, t = -7.79, p <0.001) and the reduction in HS was 1.68 Kgf (EP = 0.147, t = -11.89, p <0.001). The calculated effect size for these differences in the LOS >7 group was r = 0.40 and r = 0.56, respectively.

Length of Hospital Stay

In the univariate analysis, the number of days that the patient spent in the emergency room (ER) was statistically associated with a longer period of general hospitalization [HR = 1.16, 95% CI (1.06-2.06)], being malnourished at the time of general hospitalization [HR = 1.89, 95% CI 1.11 -3.20)], losing more than 5% of body weight during hospitalization [HR = 5.03, 95% CI (2.38-10.64)] and losing 5–10% of HS during hospitalization [HR = 3.10, 95% CI (1.99 -4.80)].

Logistic regression analysis based on the group of individuals who remained in hospital for more than seven days is shown in **Table 3**. In model 1, after adjustments, the number of days prior to hospitalization (ER period), the WL greater than 5–10% and the reduction of HS were associated with LOS >7 days [HR = 1.11 (95% CI 1.03-1.25); HR = 3.46, (IC 95% 1.58-7.59); HR = 2.48, (IC 95% 1.57-3.93)], respectively. When we included nutritional status (model 2), malnutrition and loss of HS (5–10%) remained associated with prolonged LOS [HR = 2.58, (95% CI 1.3-5.9), p = 0.02 and HR = 7.04, (95%CI 1.61-13.74), p = 0.009, respectively].

Mortality

Overall mortality in up to two years was 27.4% (n=169) for the entire group of patients and 30.3% among those hospitalized for more than seven days (vs. 19% for LOS≤7, p=0.032). There was no statistical difference regarding the reason for hospitalization between the groups.

Mortality was assessed after two years of hospital discharge (**Table 4**). The variables associated with mortality after hospital discharge were LOS >7, presence of T2D and malnutrition, which remained associated with mortality even after adjustments [HR: 1.75, (95%IC 1.57-2.33), HR: 1.45, (95%IC 1.05-2.05), HR: 1.28 (95%CI 1.10-3.05)].

In the analysis of survival, we evaluated the relation between two years of mortality with the nutritional status stratified by the presence of T2D (**Figure 1**). Individuals with T2D who were malnourished or at risk of malnutrition have a shorter survival time than the older patients with T2D with adequate nutritional status (p = 0.024).

When we evaluated the LOS according to gender **(Figure 2**), the risk of mortality was higher for men only when they stayed longer than seven days (p = 0.048). In relation to nutritional status, women with adequate nutritional status had a longer survival time when compared to women at risk of malnutrition or already malnourished (p = 0.010); in men, the nutritional status was not determinant (Figure 3).

Discussion

Our study evaluated the loss of muscle strength and body weight during hospitalization as possible predictors of LOS and mortality after discharge. Most patients already had significant muscle weakness at the time of hospital admission and lost an average of 1.68 kgf during hospitalization. Patients who remained in hospital for more than seven days had a mean loss of HS higher than those who stayed for a shorter period. Unintentional WL also contributed to longer hospitalization, there was an average reduction of 1.45 kg between patients who remained for more than seven days (vs. 0.48 kg in the group that remained less time), with no difference in baseline weight between the groups.

Each day in the ER increased the chance of staying in the hospital for longer than seven days by 11%. However, this reflects only a local condition, where the most severely affected patients are waiting for a period in the ER prior to being transferred to the ward. The less severely affected patients are discharged directly from the ER.

When evaluated the association between LOS and the percentage of loss of HS during hospitalization, it was found that prolonged hospitalization was associated with a reduction in HS of 5–10% (HR = 7.04; p = 0.009). Recent publications emphasize that there is already a loss of muscle mass in older patients within one week of hospitalization[18]. This becomes even more important when the older patients already have a muscle mass below the ideal level for their age. In the present study, the mean HS was already below the cut-off point for both sexes at admission (24.6 ± 6.8 kgf in men and 16.30 ± 5.5 kgf in women). Individuals with reduced muscle strength at hospital admission demonstrate an inverse association with length of hospital stay according to a meta-analysis performed with patients aged over 65 years old[19]. Prolonged hospitalization time is associated with a higher rate of re-hospitalization[20], poorer nutritional status[21] and mortality, with frequent re-hospitalization being associated with the risk of death[22,23].

In our sample, malnutrition and hospitalization time greater than seven days proved to be predictors of mortality, as did the presence of T2D. Similarly, Allard et al.[6] evaluated the nutritional status of 424 older patients with LOS ≥7 days, of which malnutrition was associated with longer hospital stays and higher mortality. In the same study, 50.9% of the group was already malnourished at admission. Likewise, other studies[7,24] conducted with adult individuals corroborate the finding that there is a positive association between malnutrition and length of hospitalization compared to well-nourished patients. In addition, well-nourished patients appear to be protected from prolonged hospitalization, according to Correia et al. [HR = 0.70, (95% CI 0.59-0.83)].

We found no association between the percentage loss of HS and mortality, although among the 20.3% of deaths in the study, 62% of older patients had a HS score below that recommended at hospital discharge. A systematic review showed that the reduction of HS was inversely related to cardiovascular disease mortality in studies with a follow-up of 2.5 to 24 years[25]. Our study showed a negative result between HS and mortality, because this outcome needs longer follow-up [26,27] than our study does.

Among subjects with T2D, being well nourished was decisive to increase survival in the evaluated time. Recent results agree with this finding, since malnutrition was associated with an increased risk of cardiovascular events in older patients with T2D [28]. Therefore, our result emphasizes that it is necessary to ensure that the patient has in adequate nutritional status in the third age, since malnutrition has a negative impact on older patients with T2D.

The study presents limitations because it is a sample of specific older patients from the south of Brazil who were treated in a public hospital. Since the follow-up after discharge from hospital was performed by telephone contact, it was not possible to determine whether the patients had changed their nutritional status and/or their HS during the post-discharge period, which are factors that contribute to mortality. However, our study is prospective with follow-up period of two years. Another important finding refers to the reduction of HS during hospitalization, which it is normally an instrument that is used only for screening functional and nutritional status and it is rarely used as a dynamic variable during hospitalization.

Our study demonstrated that older people who lost more weight during hospitalization and who reduced HS remained hospitalized for longer. Additionally, hospitalization time and nutritional status of the older patients, as well as having T2D and being malnourished, were important risk factors for mortality.

Preventive measures focused on preserving the muscular mass of older patients could be taken during hospitalization to minimize risks related to malnutrition, as well the inclusion of instruments to early screening of nutritional status at the admission and during follow-up.

Acknowledgment

We would like to thank all the hospitalized patients who agreed to participate in this study and to Instituto Nacional de Desenvolvimento Científico e Tecnológico (CNPq), MVB have received a scholarship from CNPq.

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Tabela 1. Characteristics of older patients stratified by length of hospital stay

Variable	All patients (610)	> 7 days (459)	< 7 days (151)	p-value
Age (years)	71.35 ± 6.45	71.08 ± 6.29	71.67 ±6.59	0.26
Women (%)	314 (51)	234 (51.0)	76 (50.3)	0.92
Caucasianos (%)	475 (77.1)	356 (77.6)	116 (76.8)	0.84
Education (elementary school)	469 (73.2)	317 (69.1)	97 (64.2)	0.66
Smokers (%)	91 (14.8)	49 (54.0)	42 (46.2)	0.56
Alcoholics (%)	82 (13.3)	34 (41.5)	48 (58,5)	0.35
Sedentary (%)	555 (90.1)	405 (88.2)	132 (87.4)	0.77
T2D (yes) (%)	312 (50.6)	230 (50.3)	80 (53)	0.57
Presence of neoplasia (%)	171 (27.8)	84 (49.1)	87 (50.9)	0,5
Days in Emergency	1.4 (0-2)	1.75 (0-3)	1,08 (0-2)	<.001
Albumin (g/dl)	3.67 (1.2- 5.2)	3.6 (1.4-4.8)	3,9 (1.9-5.3)	<.001
Hb A1c (%)	6.71 ± 1.90	6.73 ±2.0	6.69 ±1.80	0.80
More than 5 drougs (%)	146 (23.7)	74 (50.7)	72 (49.3)	0.63
weight at admission (Kg)	69.12 ± 15.25	71.03 ± 15.13	70.63 ± 15.18	0.51
weight at discharge (Kg)	68.0 ± 15.10	69.58 ± 15.01	70.15 ± 16.07	0.79
%WL (>5%)	117 (19)	112 (21.6)	5 (5.4)	<.001
MNA -Eutrófic (%)	216 (35.5)	156 (33.7)	60 (41.4)	0.03
MNA- Risk of malnutrition (%)	250 (41.1)	184 (39.7)	66 (45.2)	
MNA- Malnutrition (%)	143 (23.5)	123 (27)	20 (14)	
HS (admission)Kgf	20.40 ± 7.46	20.4 ± 7.05	20.6 ±7.74	0.23
HS (discharge)Kgf	18.81 ± 7.81	18.72 ± 7.44	20.07 ±8.03	.007
HS (loss of muscle strength) (%)	264 (43.2)	228 (49.6)	36 (24)	0.01
IADL (points))	7 ± 1.7	5 ± 1.8	7 ±1.6	<.001
Mortality (%)	169 (27.4)	140 (30.3)	29 (19)	0.032
Cardiovascular Disease (%)	129 (21)	68 (25.2)	62 (21.3)	0.68
Neoplasias (%)	117 (19)	52 (19.3)	68 (23.4)	
Infection disease (%)	44 (7)	23 (8.5)	17 (5.8)	
Complications of T2D (%)	20 (3.2)	11 (4.1)	4 (1.4)	
Others	73 (12)	30 (11.1)	45 (15.5)	

Data are expressed as mean±standard deviation, median (interquartil interval) or n (%),

T2D: type 2 diabetes; Hb A1c: glycated hemoglobin;WL : weight Loss; HS:handgrip strength; IADL: Instrumental Activities of Daily Living

Table 2. Difference in weight and muscle strength, stratified by length of hospital stay

	<7 days (n=151)						>7days (n=459)					
	Mean	**Dif**	**SE**	**t**	**CI 95%**	**p**	**Mean**	**Dif**	**SE**	**t**	**CI 95%**	**p**
Weight at admission (Kg) Weight at discharge (kg)	70.63 70.15	- 0.48	0.13	3.67	0.22-0.74	<0.001	71.03 69.58	-1.45	0.13	8.13	0,80-1.31	<0,001
HS at admission (Kgf) HS at discharge (Kgf)	20.66 20.07	- 0.59	0.15	4.05	0.30-0.88	<0.001	20.4 18.72	-1.68	0.11	12.0	1.05-1.47	<0,001

Dif: difference between the mean-CI: confidence interval 95%- SE:standard error

HS:handgrip Strength

Table 3. Analyses univariate and multivariate logistic regression of factors associated with length of hospital stay

	Univariate			**Multivariate -Model 1**			**Multivariate-Model 2**		
	HR not adjusted	**CI (95%)**	**p-value**	**HR adjusted**	**CI (95%)**	**p-value**	**HR adjusted**	**CI (95%)**	**p-value**
Age (years)	0.98	0.95-1.00	0.14	0.97	0.94-1.00	0.10	0.99	0.95-1.04	0.94
Gender (Women)	1.07	0.73-1.57	0.69	1.19	0.78-1.81	0.40	1.26	0.73-2.17	0.40
Presence of neoplasia	1.24	0.81-1.89	0.30	1.23	0.78-1.93	0.35	1.38	0.75-2.53	0.29
Presence of T2D	0.84	0.56-1.25	0.19	0.91	0.60-1.15	0.54	0.79	0.53-1.61	0.79
IADL	0.72	0.48-2.53	0.17	0.83	0.45-1.89	0.12	0.96	0.47-1.18	0.13
Days in ER	1.16	1.06-2.06	0.001	1.11	1.03-1.25	**0.011**	0.99	0.89-1.09	0.85
WL (>5%)	5.03	2.38-10.64	<0.001	**3.46**	1.58-7.59	**0.002**	**---**	**---**	**---**
MNA (malnutrition)	1.89	1.11-3.20	0.017	**---**	**---**	**---**	**2.58**	**1.13-5.90**	**0.02**
HS (≤ 5%)	1			1			1		
HS (>5; ≤10%)	3.10	1.99-4.80	<0.001	**1.88**	**1.57-3.93**	**<0.001**	**7.04**	**1.61-13.74**	**0.009**
HS (>10; ≤ 20%)	1.83	1.02-3.66	0.18	1.42	0.97-1.96	0.30	1.01	0.65-2.78	0.98
HS (>20%)	1.55	0.89-7.43	0.86	1.47	0.91-2.03	0.72	2.06	0.99-11.64	0.052

Model 1: Days in emergency, WL> 5%, HS, as predictors; adjusted for age, sex, presence of neoplasia, presence of T2D

Model 2. Days in emergency; MAN, HS as predictors, adjusted for: age, gender, neoplasia, T2D

T2D: type 2 diabetes ; IADL: Instrumental Activies of daily living; ER: emergency room; WL:weight loss; MNA: mini nutrition assessment; HS: handgrip strength

Table 4. Predictors of 2-year mortality after hospital discharge.

	Univariate			Multivariate- model 1			Multivariate-model 2		
Variables	**HR not adjusted**	**CI 95%**	**p-value**	**HR adjusted**	**CI 95%**	**p- value**	**HR adjusted**	**CI 95%**	**p- value**
Age (years)	1.01	0.99-1.04	0.19	1.01	0.99-1.04	0.22	1.01	0.98-1.04	0.24
Gender (Women)	1.21	0.83-1.53	0.44	1.076	0.78-1.48	0.65	1.09	0.79-1.50	0.60
Presence of neoplasia	1.80	1.30-2.45	0.002	1.78	1.30-2.46	0.00	**1.77**	**1.05-2.08**	**0.02**
Presence of T2D	1.37	1.03-1.87	0.04	1.46	1.07-2.00	0.018	**1.45**	**1.05-2.05**	**0.03**
Days in ER	1.074	0.98-1.20	0.05	1.08	0.99-117	0.05	1.09	1.00-1.17	0.57
LOS (>=7days)	1.20	1.02-1.37	0.03	1.61	1.11-2.35	**0.012**	**1.75**	**1.57-2.33**	**0.00**
HS (5- 10%)	1.19	0.87-2.12	0.36	--	---	**---**	---	---	---
MNA (malnutrition)	1.60	1.89-2.95	0.016	--	---	---	**1.28**	**1.10-3.05**	**0.019**

Model 1: LOS≥7 days as a predictor of mortality adjusted for age, gender, presence of T2D and neoplasia
Model 2: malnutrition as predictors of mortality adjusted for age, sex, presence of T2D and neoplasia
ER: Emergency room; LOS: length of hospital stay; HS: handgrip strength; MNA: mini nutrition assessment

Figure 1. Survival analysis according to nutritional status in patients with T2D (Log Rank=0.024)

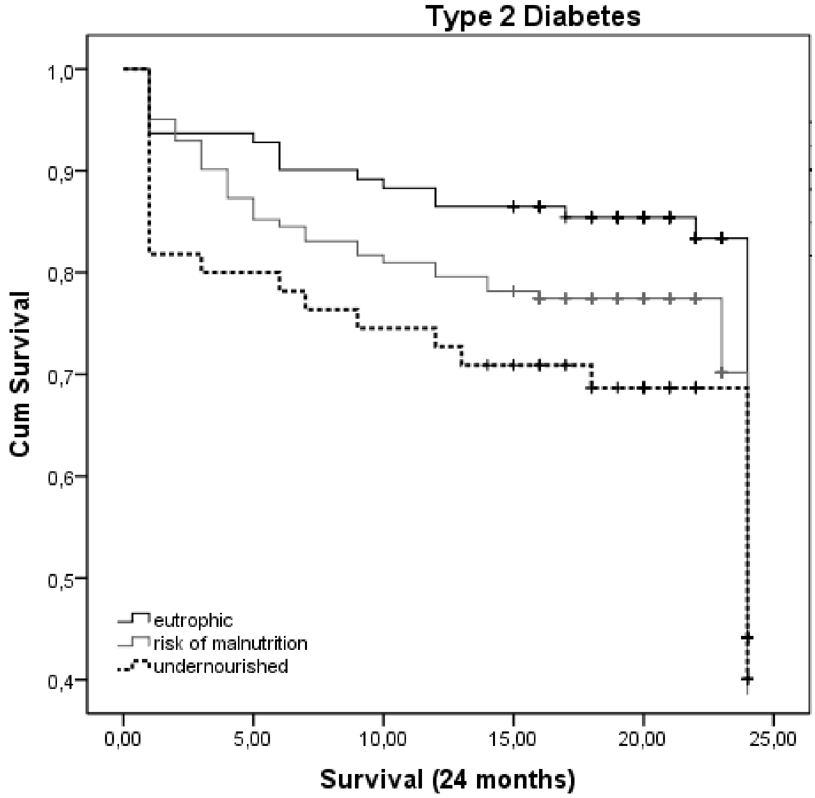
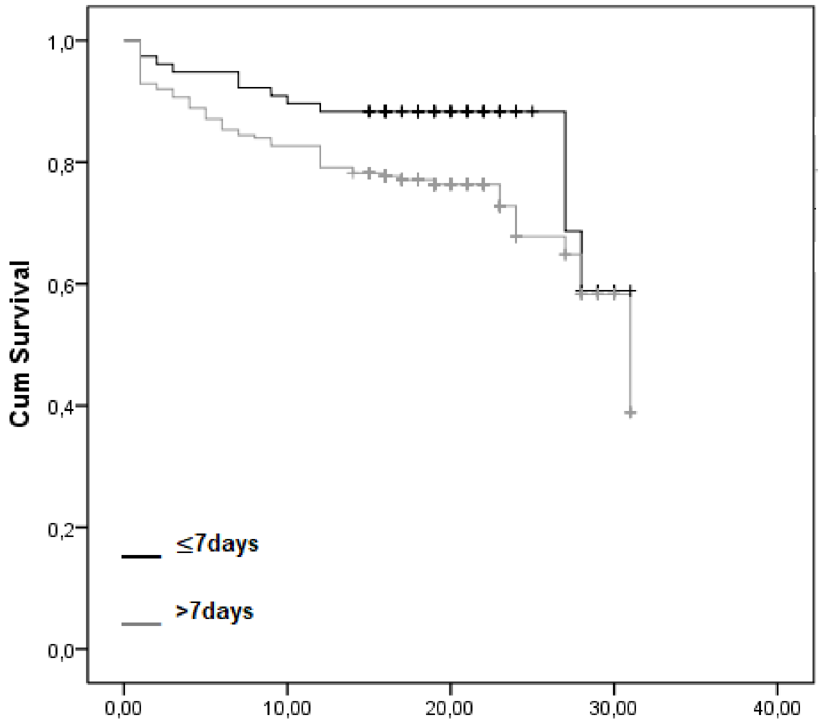


Figure 2. Survival analysis according to length of stay stratified by males (Log Rank=0.048)



CAPÍTULO III

"Adductor pollicis muscle thickness as predictor of mortality post discharge in older people"

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Abstract

Background: The adductor pollicis muscle thickness (APMT) may reflects the muscular atrophy that occur during hospitalization in older patients. The lower APMT, the greater the risk of infectious complications, poorer nutritional status and increased morbidity. The aim of this study was to investigate whether APMT is a predictor mortality for older patients after 24 months of hospital discharge.

Methods: A prospective cohort study was conducted which involved older patients (>60 years) followed during hospitalization and after hospital discharge for up to 24 months. All patients were subjected to anthropometric measurements and mini nutritional assessment. The values of APMT were divided into quartiles and were analyzed as the potential risk factors for mortality after hospital discharge.

Results: A total of 610 patients, with a mean age of 71.35 ± 6.45, 51% female, 77% white and 90% sedentary, were included in the study. There were 27.4% deaths in the follow-up period. Patients who died were more dependent on the instrumental activities of daily living, with malnutrition, higher prevalence of women (57%) and they had a lower APMT (9mm vs.12mm; p = 0.006), being 47% of them in the first quartile (4-8 mm).

Conclusions: Patients with the measurement APMT in the lower quartile had higher mortality risk after 24 months of hospital discharge

Keywords: adductor pollicis muscle thickness; mortality; malnutrition.

Introduction

It is known that muscle mass loss is part of the natural physiological aging process and this decline impairs the functional capacity of the individual. In older people, this reduction is even more accelerated, and muscle mass loss up to 10% can occur within 7 to 10 days of bed rest [1]. Changes in nutritional status during hospitalization requires some days to be identified. However, variations related to functional status appear earlier, such as the handgrip strength and the adductor pollicis muscle thickness (APMT), both demonstrates muscle mass loss related to the period of muscular inactivity[2]. The loss of muscle function is a predictor of morbidity and mortality in hospitalized adults[3].

The APM is the only muscle that allows direct evaluation through its thickness [2], due to its location between the two bones of the hand; it is easy to apply without needing specialized formulas.

The APMT is an evaluation method that is fast, non-invasive and may reflecting the loss of muscle atrophy[2,5,7-9]. Nevertheless, the relationship between APMT and mortality after hospital discharge in older patients is unknown.

Thus, the objective of this article was to evaluate the APMT from dominant hand as a mortality predictor after 24 months of hospital discharge.

Methods

Sample and study design

A sample of 610 patients of both sexes, aged over 60 years, hospitalized in a clinical ward of a university hospital in Southern Brazil was evaluated from July 2015 to December 2016. Were included patients older than 60 years old, with up to 48 hours of hospital admission, who agreed to participate in the study and signed the consent form. Were excluded patients who did not deambulate, those with any amputation, mental decline or advanced motor sequalae; those who were treated at the Intensive Care Unit, and those who were in hospital for less than two days. The questionnaire was applied to evaluate information such as: age, gender, marital status and social status. The patients were approached during their hospitalization first 48 hours in the ward unit.

All patients were followed up during hospitalization and after hospital discharge for up to 24 months and were contacted by telephone regarding their health state and their medical records were verified every three months after discharge.

Demographics, clinical data, medical diagnoses, and admission data were obtained through questionnaires and by consulting the patient's clinical file. This research was performed according to the recommendations established by the Declaration of Helsinki and approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre (# 150068).

The patients' nutritional status was evaluated in the admission through the Mini Nutritional Assessment (MNA). The patients were classified according to the cut points proposed in a previous study: (eutrophic 24 to 30 points, risk of malnutrition with 17 to 23.5 points and malnourished<17 points)[10]. The height was measured by a stadiometer (**Standard** Sanny SKU) and the weight was measured by a digital scale (Uranus-UR10000), both were measured at admission. All anthropometric measurements were performed by two nutritionists certified in anthropometry (ISAK2).

The APMT was performed according to proposed technique per Lameu et al[2] : patients sat with both arms relaxed and elbows in a 90-degree angle, approximately, with the hands laying over the legs, was measured by skinfold caliper (Lange®), in the vertex of an imaginary triangle formed by the extension of the thumb and the index finger, under a continuous pressure of 10 g/mm. The average of 3 measurements of the dominant hand was considered as the average adductor muscle thickness.[11]

To evaluate the independence level, the Instrumental Activities of Daily Living test (IADL)[12] was performed. The IADL is a scale that assesses eight tasks providing information about functional skills necessary to live independently in the community. Each activity can be scored as either 1 (can perform task independently) or 0 (not able to do), a score ranges from 0 (low function, dependent) to 8 (high function, independent). [12]

Statistical Analysis

The sample size was calculated by using the free software G* Power 3.1 (Heinrich-Heine University Düsseldorf, Düsseldorf (NRW), Germany[13]. All variables had normality assessed by Kolmogorov-Smirnov test, the results were described as average and standard deviation or median and interquartile range (IQR). Categorical variables were reported as frequencies. T test for independent variables for parametric variables or Mann Whitney for non-parametric variables were performed, chi-square test for categorical variables.-Survival curves were analyzed according to Kaplan-Meier to explore the APMT impact on survival. Differences between curves were evaluated using the log-rank test. The APMT was divided according to the quartiles value among all patients (1º quartil: 2 -8mm, 2ºquartil: 9-10mm, 3º quartil: 11-13mm and 4ºquartil:

14-26 mm). Cox regression models, hazard ratio (HR) with 95% confidence intervals (CI) using the mortality as dependent variables. The models were adjusted for age, gender, neoplasia, hospitalization length and independence level. Statistical significance was defined as $P < 0.05$. All analyzes were performed with the Social Science Software Package (SPSS) for Windows (version 20.0; SPSS, Inc., Chicago, IL, USA). For the sample calculation, we included patients consecutive admitted to the clinical unit under study from July 2015 to February 2016.

Results

Of the 616 patients included in the study, six discontinued from participating in the study after discharge. The average age was 71.35 ± 6.45, 51% were females, 77% withe, 90% sedentary. Type 2 diabetes (T2D) and hypertension were present in 50.6% and 70.1%, respectively. The participant's characteristics at baseline were described in Table 1 and were stratified by mortality up to 24 months from hospital discharge. There were 169 (27.4%) deaths in the follow-up period. Among the patients who died, there was a higher prevalence of women [96 (57%) vs. 217 (49%), p = 0.05]; the most common disease was malignant neoplasia (67 [42%] vs. 105 [25.6], p = 0.001) compared to those who lived. In addition, they were more dependent on the daily living instrumental activities (4.13 ± 1.86 vs. 6.06 ± 1.73; p = 0.04), more undernourished (28 [37.3%] vs. 115 [21.5%], p <0.001), had lower levels of serum albumin (3.48 [3.2-4.0] vs 3.67 [3.3-4.2]), had a lower APMT (9.12 ± 3.76 vs. 10.58 ± 4.28, p = 0.006) and 78 (47%) of them were in the first quartile [vs. 141 (32%), p<0.001].

Malnutrition patients had a lower APMT compared to eutrophic patients. **Figure 1** describes the median APMT according to the nutritional status by the dominant hand (in normal: 11; risk of malnutrition: 10 mm, malnutrition 8 mm, p <0.001). A Kruskal-Wallis test provided evidence of a difference (p < 0.001) between the mean ranks of at least one pair of groups. Dunn's pairwise tests were carried out for the three pairs of groups. There was very strong evidence ($p < 0.001$, adjusted using the Bonferroni correction) of a difference between the group risk of malnutrition and malnutrition, and normal and malnutrition. The median AMPT for the group normal was 11mm compared to 8mm in the group malnutrition. There was no evidence of a difference between risk of malnutrition and normal.

Multivariate analyzes between post discharge mortality and possible predictors were described in **Table 2**. The models were adjusted for age, gender, presence of neoplasia, independence level, and length hospital stay. In model 1, patients with an APMT in the first quartile (2-8mm), had a mortality risk of 1.63 after hospital discharge, when compared to patients with higher quartile (14-26mm). The same was observed in model 2, of which malnutrition was included, risk for 1º quartile of APMT [OR: 1.65; IC (1.02-2.74); p = 0.043]. In model 3, we analyzed as single variable the presence of malnutrition plus being in the first quartile of APMT, and the patients with both presented a 70% risk for mortality.

A Kaplan-Meier curve was performed (**Figure 2**) to assess the relation between quartiles of APMT and post hospital discharge survival (log rank = 0.016).

Discussion

This study investigated the relationship between APMT and mortality after hospital discharge within 24 months in older patients. Patients who presented APMT in the first quartile, in comparison to the higher quartiles, had a higher risk of mortality after hospital discharge. In addition, malnourished patients with APMT in the first quartile (thinner) were at high risk of mortality after discharge.

The APMT has been evaluated in other studies with hospitalized adults and older [2, 9, 14, 11, 16] and in the healthy population[17] because it is a localized muscle between two bone structures, is a fast, easy-to-access, low-cost method[2]. The APMT reflects the patient's own independence to perform daily activities. In fact, muscle mass reduction is associated with worse outcomes, but the decline in muscle strength and functional has been the best predictor of morbidity and mortality in the older people.

Previous studies have shown that the lower the thickness the greater the risk of complications and worse outcomes, such as: longer hospital stay length[2,16], more days of mechanical ventilation use[9] and in-hospital mortality[4,5,9]. In addition, the measure can be used to assess nutritional risk in critically ill patients[18] and surgical patients.[6,15]

Regarding the APMT association and mortality, previous studies [9,5,19] associated the lower APMT with mortality under different conditions. Caparossi et. al [9] in his study with surgical patients showed that among patients who died, APMT values were significantly lower (11.4 ± 4.1 in the right hand and 11.2 ± 3.9 in the left p = 0.03). Likewise, Bragnolo et al. [5] showed that postoperative mortality was 25% higher in patients with APMT below the cut-off point considered for dominant hand in the older patients <12.2mm (women) and <14.4mm for men and Ghorabi et.al [19] in patients from intensive care unit, 11.12 ± 2 mm in the patients who died and 16.7 ± 2.2 mm in those who survived (P = .05). However, Pereira et al.[20] and Shu-fen et al.[21] found no relation between APMT and mortality, but this last study was a cross-sectional study with a population different from the Brazilian population.

We evaluated the relationship between nutritional status and APMT. In our sample it is possible to observe that patients malnourished or at nutritional risk presented lower APMT in both hands, similar results were found by Gonzalez MC et al.

[11]. Other studies have shown a good correlation of APMT with BMI [11,18], with handgrip strength[22] and with other anthropometric measurements, such as arm muscle circumference [22]. In our sample, we had a positive but weak correlation between APMT and calf circumference (r = 0.30), arm muscle circumference (r = 0.34) and handgrip strength (r = 0.28). We chose to use MNA to assess nutritional status because it is a tool that better detects malnutrition or the risk of malnutrition in hospitalized older people.[10]

The dependence level also showed an evident association with mortality after 24 months of hospital discharge. The more dependent older patients (with less than 8 points in the IADL) had a higher mortality rate when compared to the independent patients; the association between IADL and mortality already described for other authors. [23,24]

In our study, the thickness measurement was performed in both hands, but we chose to present only the dominant hand analysis because it is the one that most demonstrates muscle loss with lack of activity. The dominant hand evaluation is preferred over non-dominant, since the most exercised muscle tends to shrink more rapidly in a situation of malnutrition [17].

As a possible limitation, the APMT measurement was performed only once, 48 hours after admission, and it was not possible to assess whether the patients further reduced the thickness during hospitalization.

As strength of our study, we highlight the prospective design, as well as the significant number of patients evaluated for a significant time after hospital discharge. It is becoming increasingly important to include the assessment of muscle mass and functionality in the older individual as a complementary way to nutritional assessment.

In summary, this study demonstrates that APMT is easy and can be evaluated in older patients hospitalized at the bedside, besides it is possible being used as an auxiliary evaluation of the nutritional evaluation that allows to verify patients at risk of mortality.

Acknowledgment

We would like to thank all the hospitalized patients who agreed to participate in this study, to students of scientific initiation Juliane Feldman and Camila Nery and to Instituto Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

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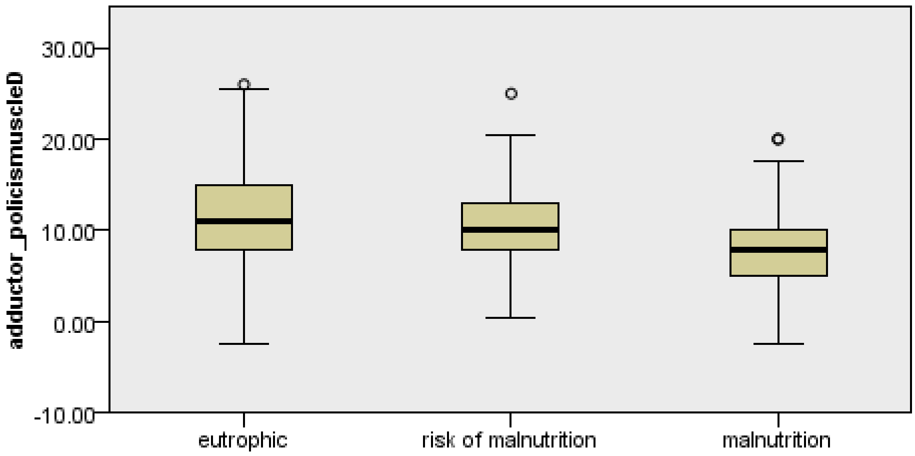
Table 1. Clinical and nutritional characteristics of older patients stratified by mortality

Variables	All patients (n=610)	Mortality (n=169)	Alive (n=441)	p-value
Age (years)	71.35 ± 6.45	72.17 ± 6.52	71.23 ± 6.44	0.23
Gender (Women)	314 (51)	96 (57)	217 (48.5)	0.04
Caucasian	474 (77.1)	127 (75)	347 (78)	0.84
Elementary School	469 (77.1)	347 (78)	122 (71.4)	0.13
Smokers	91 (14.8)	20 (22)	71 (78)	0.02
Alcoholics	82 (13.3)	21 (25.6)	61 (74.4)	0.46
Sedentary	555 (90.1)	66 (88)	486 (90.4)	0.51
T2D (yes)	306 (50.6)	97 (57)	209 (48)	0.05
Presence of neoplasia	171 (27.8)	67 (42)	105 (25.6)	.001
Presence of SAH	432 (70.1)	46 (61.3)	386 (72.3)	0.05
SBP (mmHg)	129.86 ± 19.95	126.39 ± 19.82	130.34 ± 19.31	0.11
DBP (mmHg)	72.09 ± 11.69	70.28 ± 10.92	72.35 ± 11.78	0.15
Albumin (g/dl)	3.7 ± 0.64	3.48 (3.2-4.0)	3.67 (3.3-4.2)	0.01
Hb A1c (%)	6.71 ± 1.90	6.91 ± 1.91	6.59 ± 1.89	0.08
More than 5 drougs	147 (23.7)	40 (23.5)	107 (24)	0.48
IADL (score)	6.13 ± 1.17	5.17 ± 1.69	6.04 ± 1.83	.002
Score (men)	5.6 ± 1.7	5.41 ± 1.87	5.7 ± 1.61	0.22
Score (women)	6.1 ± 1.8	4.13 ± 1.86	6.06 ± 1.73	0.04
LOS >7 days	301 (48.9)	46 (15.3)	255 (84.7)	0.02
MNA (malnutrition)	143 (23.44)	58 (34.3)	85 (19)	0.006
APMT (mm)	11 (8-13)	9 (6-11)	12 (8-14)	.006
1º quartil (2-8mm)	219 (35.4)	78 (47)	141 (32)	<.001
2º quartile (9-10m)	140 (22.7)	43 (26)	97 (22)	
3º quartile (11-13mm)	110 (18.0)	23 (14)	87 (19.7)	
4º quartile (14-26mm)	140 (22.7)	23 (13,8)	117 (26.5)	
Causes of hospitalization				
Cardiovascular disease	130 (21)	32 (20.3)	98 (24.3)	0.48
Neoplasias	120 (19.5)	43 (27.2)	77 (19.1)	

Data expressed as mean ± SD; median (Interquartile Range) or n (%). T2D: type 2 diabetes; SAH: systemic arterial hypertension; SBP: systolic blood pressure; DBP: diastolic blood pressure; Hb A1C: Glycated hemoglobin; IADL: instrumental activities of daily living; LOS: length of hospital stays; MNA: mini nutrition assessment; adductor pollicis muscle thickness (APMT).

Figure 1. Adductor pollicis muscle thickness according to the nutritional status.



Independent Samples- Kruskal-Wallis test p<0,001.

Dunn's pairwise tests

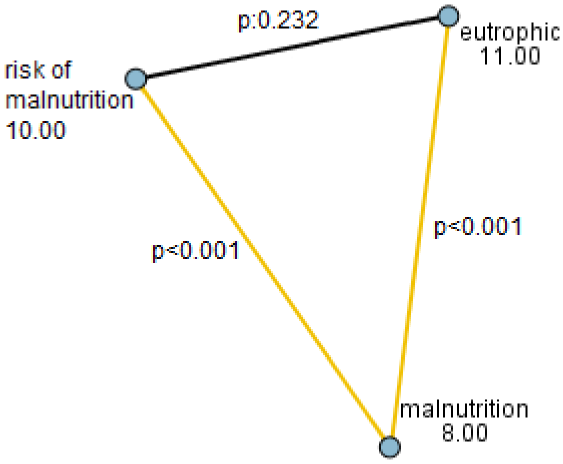


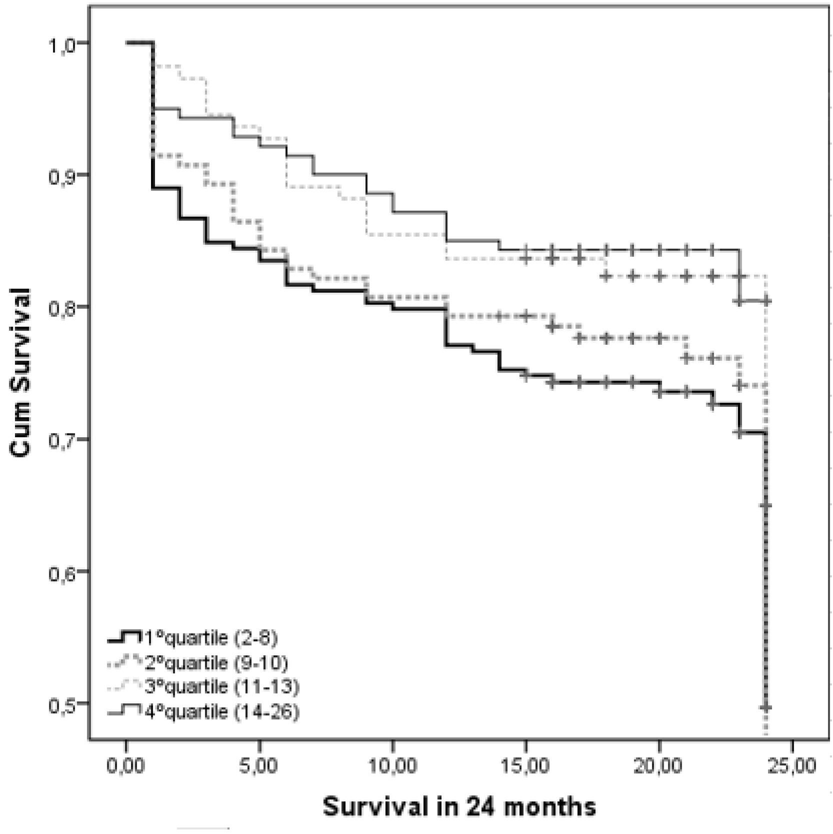
Table 2. Univariate and multivariate Cox regression analysis of variables associated mortality.

	Univariate			Multivariate Model 1			Multivariate model 2			Multivariate model 3		
Variables	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Age (years)	1.02	0.99-1.040	0.20	1.06	0.98-1.03	0.62	1.00	0.98-1.03	0.70	1.01	0.98-1.03	0.44
Gender (male)	1.12	0.83-1.53	0.44	1.02	0.73-1.42	0.89	1.01	0.73-1.40	0.95	1.06	0.76-1.46	0.72
Woman	1			1			1					
Neoplasia (yes)	1.80	1.30-2.46	0.001	1.71	0.73-1.42	0.00	1.67	1.20-2.30	0.002	1.77	1.30-2.44	0.00
No	1			1			1					
LOS (>7days)	1.25	0.80-1.96	0.32	1.25	0.77-2.02	0.36	1.22	0.75-1.98	0.42	1.26	0.77-2.03	0.35
<7 days	1			1			1					
IADL (dependent)	1.44	1.01-2.05	0.04	1.43	0.99-2.06	0.06	1.37	0.95-2.00	0.09	1.42	1.01-2.04	0.54
(Independent)	1			1			1			1		
MNA (malnutrition)	1.58	1.03-2.34	0.02				1.36	0.91-2.01	0.13			
Normal	1						1					
APMT (1° quartile)	1.70	1.05-2.73	0.03	1.68	1.026-2.76	0.03	1.65	1.12-2.74	0.03			
2° quartile	1.72	1.02-2.83	0.04	1.52	0.89-2.60	0.12	1.50	0.88-2.56	0.13			
3° quartile	1.22	0.66-2.12	0.55	1.06	0.58-1.95	0.83	1.38	0.66-2.80	0.62			
4° quartile	1			1			1					
Malnutrition+ 1°quartil	1.53	1.04-2.24	0.03							1.70	1.11-2.53	0.01

All the multivariate models were adjusted to: age, gender, presence of neoplasia, LOS and IADL.

HR: hazard ratio; CI: confidence interval; APMT: adductor pollicis muscle thickness; MNA: mini nutrition assessment; LOS: length of hospital stay; IADL: instrumental activities of daily living.

Figure 2. Kaplan-Meier curve of quartiles for APMT and post hospital discharge (log rank = 0.016).



CAPÍTULO IV

"Sarcopenia and Type 2 diabetes mellitus as predictors of mortality after hospital discharge in a cohort of hospitalized older adults: 2 years of follow-up"

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Abstract

Introduction: Sarcopenia has been discussed as a possible predictor of mortality in the older people, but there are few studies evaluating the relationship between mortality and sarcopenia in the population of patients with T2D, especially after hospital discharge. **Objective**: To verify the predictors of mortality within 2 year after hospital discharge in patients with and without T2D. **Methodology:** A prospective study that included patients hospitalized at the Hospital de Clínicas of Porto Alegre (HCPA) between July 2015 and December 2017, over 60 years and with up to 48 hours of hospitalization in a ward unit. To assess sarcopenia, a 3-meter gait test was performed, such as Time Up and Go, muscle strength was measured by handgrip using an analog dynamometer, and muscle mass was measured across the largest calf circumference region. Patients with reduced gait (<0.8m / s), with low muscle strength by the dynamometer (<20Kgf for women and <30Kgf for men) and lesser calf circumference (<33cm for woman and <34 for men) were considered sarcopenic. This project was approved by the HCPA Ethics Committee under number 150068. Results: 610 patients were included, mean age 71.31 ± 6.45 of which 51% were women, 77% were Caucasian. The group was stratified according to the presence of diabetes, 306 (51%) patients had TD2. Patients with T2D had lower muscle strength (19.62 ± 7.53 vs. 21.19 ± 7.31 p = 0.009), were slower in "timed up and go" teste (0.54m / s (0.46-0.66) vs. 0.60 (0.48-0.75) p <0.001) than those without T2D, 46.5% being classified as sarcopenic. The mortality rate among T2D was 28%. In the multivariate analysis after adjustment for age, sex, presence of neoplasia, BMI, level of independence and Charlson index> 2 points, when compared to the control group, the coexistence of T2D and sarcopenia was independently associated with mortality after hospital discharge (HR: 1.78; 95% CI: 1.06-2.30). **Conclusion**:

Older patients with T2D and sarcopenia had a higher risk of mortality after hospital discharge compared to a control group.

Keywords: sarcopenia, type 2 diabetes, mortality

Introduction

The reduction of muscle mass and the consequent loss of muscle function are characteristics of aging[1], but the progressive reduction of muscular mass associated with the reduction of muscle strength gives rise to Sarcopenia[2]. Sarcopenia can directly influence the daily life of the older, leading to increased dependence, risk of falls and mortality[3]. Physical inactivity during hospitalization is almost an accepted part of the hospitalization experience, but it clearly contributes to several negative outcomes, including a reduction in the ability to perform activities of daily living, a higher incidence of readmission and institutionalization[4,5].

Individuals with type 2 diabetes (T2D) present an accelerated and early decline in muscle mass and strength, as well as poor muscle quality when compared to non-diabetic subjects [6,7], and the presence of sarcopenia in individuals with T2D increases the risk of falls and fractures[3].

The importance of assessing muscle mass in the older patient in the hospital setting was recently described as one of the diagnostic criteria for assessing malnutrition in the Global Leadership Initiative on Malnutrition (GLIM) guideline[9,10]. Data from relationship of sarcopenia in older patients with T2D and mortality after hospital discharge are scarce.

The objective of this study was to evaluate whether coexistence of sarcopenia and T2D predicts mortality after two years of hospital discharge in older patients compared to a control group without diabetes.

Methods

This study was conducted in a university hospital in the South of Brazil and had its protocol approved by the ethics committee of the Hospital de Clínicas of Porto Alegre, all participants signed an informed consent term.

All patients aged over 60 years hospitalized from July 2015 to December 2016 were considered eligible. We did not include people with neurological sequelae, those who could not walk and those who could not communicate. Selection data can be seen in the flowchart (Figure 1).

A general questionnaire was applied to evaluate data such as income, socioeconomic situation, besides consulting the medical record for admission data, registration of falls and Morse questionnaire score. Two trained nutritionists performed the anthropometric and sarcopenia-related data collection within 48 hours of hospital admission. The measured data were: weight, height, calf circumference (CC), timed up and Go" test (TUG) and handgrip strength (HS).

The TUG required patients to stand up out of the chair, walk 3 m, turn around, walk back to the chair, and sit down. Patients were given the following instructions: “stand up on the word ‘go,’ walk to the tape, turn around, walk back to the chair, and sit down.” The timing of the test began at the word “go,” and ended when the participant was seated. This course is timed and the cutoff points> 0.8m / s were used to consider the patient with low mobility [11]

Two measurements of the CC of the right leg were performed alternately with inextensible tape measure (Cerscorf, Brazil) by trained and standardized interviewers. The subject was instructed to stand with his legs apart and positioned approximately 20 cm apart. The measurement was taken at the point of greatest horizontal circumference

[12]. The mean of the two right calf measurements was used for analytical purposes. CC of ≤34 cm (ill) and ≤33 cm (females) were indicative of low muscle mass [13].

The nutritional status was evaluated through the body mass index (BMI) for the older patient. The cutoff points were: 22km / m^2 for malnourished, 22-27 for eutrophic and> 27 for overweight. Other covariates were collected through the Hospital information system through patient records and questionnaires. Age, sex, educational level, physical activity, smoking, alcohol consumption and medication. We evaluated the instrumental activities of daily living (IADL) to estimate the independence of the patient, considering individuals with scores <8 [15]. The falls that occurred at admission were assessed by consulting the medical record, while the falls after hospital discharge were questioned via telephone contact, therefore they are self-referenced.

Survival data were consulted via telephone contact with all participants. The calls were made 30 days after hospital discharge and every 3 months until completing 24 months. All death events were confirmed using the local death record database. The period from the first investigation to the date of death was recorded for participants who died during follow-up, the same was performed for the all other participants.

The severity of comorbid diseases was recorded and scored according to Charlson comorbidity index (CI) and was calculated according to the scoring system established by Charlson et al.[22].

Statistical analysis

All statistical analyzes were performed in the SPSS program version 18 (SPSS Inc. Chicago, IL, USA). The normality of the variables was tested using the Kolmogorov test. Categorical data were presented in absolute numbers and percentages (%). Continuous data are presented as mean ± standard deviation and variable categories are presented as median and interquartile range. Differences between groups were compared using the chi-square test for categorical variables and Test T or Man Whitney for quantitative variables. We considered the value of $p < 0.005$ as statistically significant. Kaplan Meier curves were performed to assess the impact of sarcopenia and T2D coexistence on mortality. The differences between the curves were evaluated by the log-rank test. The mortality time was counted in months, considering the date of the first admission until the date of death. The univariate and multivariate analysis of mortality was performed using the Cox-regression model with all patients and in different models in two sub samples, obtained in detriment of the total of patients in the sample with a BMI greater than 27 and with presence of falls during hospitalization. The models were adjusted for: age, sex, presence of neoplasia, systemic arterial hypertension, BMI, level of independence and Charlson index> 2 points.

The sample calculation was based on previous study[23] we would need 518 patients, 259 with T2D and 259 without T2D. We increased the sample to 610 patients, predicting a possible loss of follow-up of around 15%. This study showed that patients with T2D had a 3-fold higher mortality than those without T2D. The estimated power was 90% with an alpha error of 5%, $p < 0.05$.

Results

Of the 616 patients included in the study, six discontinued from participating in the study after discharge. Therefore, 610 patients were included, of these 306 had T2D and 304 with no diabetes (**Figure 1**). The mean age of the patients was 71.35 ± 6.45 years and 313 (51%) were female. Sarcopenia was present in 237 (39%) patients at hospital admission. When compared to patients without T2D, subjects with T2D had more in-hospital falls (34% vs. 19%, $p = 0.001$), as well as higher risk of falls (40 points vs. 35, p = 0.006), had more overweight (54.5% vs.38%, p = 0.005), lower handgrip strength (19.62 ± 7.5 vs. 21.19 ± 7.3, p = 0.009), were slower in the walking test (0.54 vc, 0.60, p <0.001) and had more prevalence of sarcopenia (46.5% vs. 31%, p = 0.001). The data stratified by the presence of diabetes can be seen in **Table 1**. During the 2-year follow-up, 170 (28%) patients died. The causes of the deaths were: 37 (6%) for cardiovascular diseases, 50 (8%) for neoplasia, 34 (5.5%) for septic shock, 8 (2%) for lung diseases and 3 (0.5%) for other causes. Among the deaths, 31.5% had T2D + sarcopenia, 14% had sarcopenia alone, 25% had T2D only, and 30% had neither diabetes nor sarcopenia. The relationship of mortality with sarcopenia can be seen in **Table 2**. The coexistence of diabetes and sarcopenia was independently associated with mortality after hospital discharge on unadjusted analysis (HR: 1.60, 95% CI: 1.08-2.35). In adjusted analysis, when compared to the control group without diabetes and no sarcopenia, the coexistence of T2D and sarcopenia was independently associated with mortality after hospital discharge (HR: 2.04; 95% CI: 1.06-4.48). A subgroup analysis was performed without patients with BMI> 27Kg / m^2, and the risk for mortality in patients with sarcopenia plus diabetes was 4 times higher when compared to the control group (HR: 4.03, 95% CI 1.25-12.03). Survival curves categorized by the presence of sarcopenia are presented in **Figure 2**. The survival curves were statistically different by the log-rank test (p: 0.032), indicating that patients with diabetes plus sarcopenia had a higher risk of mortality when compared to the group control

Discussion

This prospective, 2-year follow-up study was the first to evaluate the relationship between T2D and sarcopenia with mortality after hospital discharge in older subjects. Our study demonstrated that sarcopenia was prevalent in patients already on admission. After adjusting for possible confounders, the coexistence of T2D and sarcopenia was a independent predictor of mortality after hospital discharge when compared to the control group. By excluding overweight patients, the risk was 4x higher for those with T2D and sarcopenia. The relationship between sarcopenia and mortality was previously described in other studies [16,17]. Vetrano et. al [16] and Pérez-Zapeda et al[17]. evaluated the mortality in individuals with sarcopenia but with no diabetes, one year after hospitalization and reported that the mortality risk was 1.59 and 2.23 times higher when compared to those without sarcopenia, respectively. Similarly, Tang et [18]. al identified sarcopenia as a predictor of 3 years of mortality in hospitalized older patients. The multicentre study Sabe (Health, well-being and aging) reported the presence of sarcopenia as a predictor of mortality in individuals over 60 years of age who were not hospitalized [18].

In fact, patients with T2D tend to have an accelerated reduction of muscle function when compared to non-diabetes[2,6,19]. The mechanisms that lead to the decrease of the muscle mass in the patient with diabetes are still not well understood, may be related to the lower activity of anabolic hormones [2], as well as the resistance to insulin by the skeletal muscle [20,21]. Park S et. al in a 3-year follow-up study reported a 30% decline in thigh muscle strength in older patients with T2D compared to the control group, and this decline was independent of weight changes over time. In addition, muscle decline in the older with T2D is independent of disease duration, metabolic control, serum vitamin D status and presence of microvascular complications.[19]

Some limitations can be observed when interpreting these data. First, to perform the diagnosis of sarcopenia, all the patients had the strength evaluated, did the walking test and measured the muscle mass and then stratified by the presence or absence of sarcopenia according to the cut-off points established in the algorithm. Muscle mass was assessed by the circumference of the calf and only one measure was measured, in this case we do not know if the patients lost muscle mass during the hospitalization period.

In summary, in a population of older hospitalized adults, those with sarcopenia and T2D had a higher risk of mortality after hospital discharge compared to patients without sarcopenia and without T2D. The evaluation of sarcopenia in the hospital context can be considered a prognostic factor for the conduct of older hospitalized adults, especially if diabetes is present.

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Figure 1. Flowchart

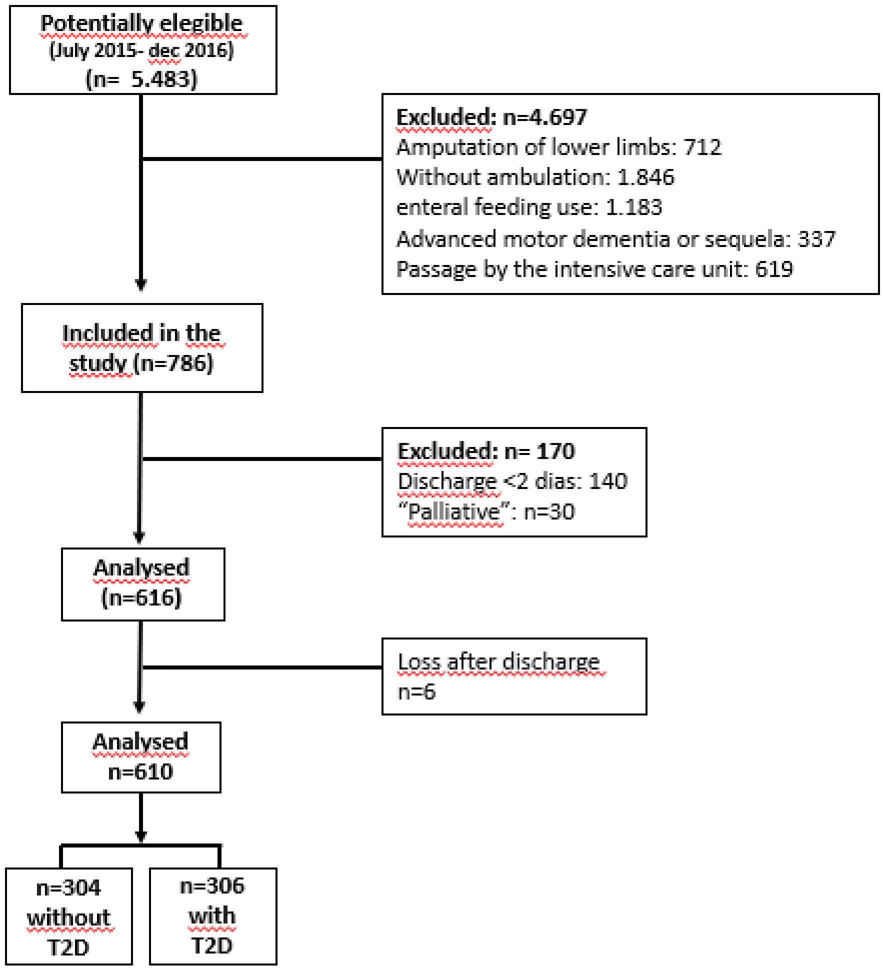


Table 1. Clinical and nutritional characteristics of hospitalized older with and without type 2 diabetes.

Variables	T2D (n=306)	No T2D (n=304)	p-value
IADL			
Dependent (<8)	227 (73.5)	167 (55.7)	**<0.001**
Independent (=8)	82 (26.5)	133 (44.3)	
Morse (falls)	40.0 (24.5-51.25)	35.0 (15-45)	**0.006**
Falls (in-hospital)	68 (34.3)	45 (19)	**0.001**
Falls (post discharge)	11 (4.5)	6.0 (2.0)	0.13
BMI			
Normal	105 (35.2)	118 (39)	**0.005**
Malnutrition	32 (10.3)	68 (22.7)	
Overweight	169 (54.5)	114 (38)	
HS (KGf)	19.62 ± 7.53	21.19 ± 7.31	**0.009**
men	23.74 ± 7.10	25.66 ± .640	**0.014**
women	15.68 ± 5.60	16.90 ± 5.30	**0.049**
Tug (m/s)	0.54 (0.46- 0.66)	0.60 (0.48-0.75)	**<0.001**
CC (<33 cm-men)	54 (33)	41 (28)	0.53
CC (<34cm -women)	82 (52)	59 (38.6)	**0.017**
Sarcopenia	144 (46.5)	93 (31)	**<0.001**

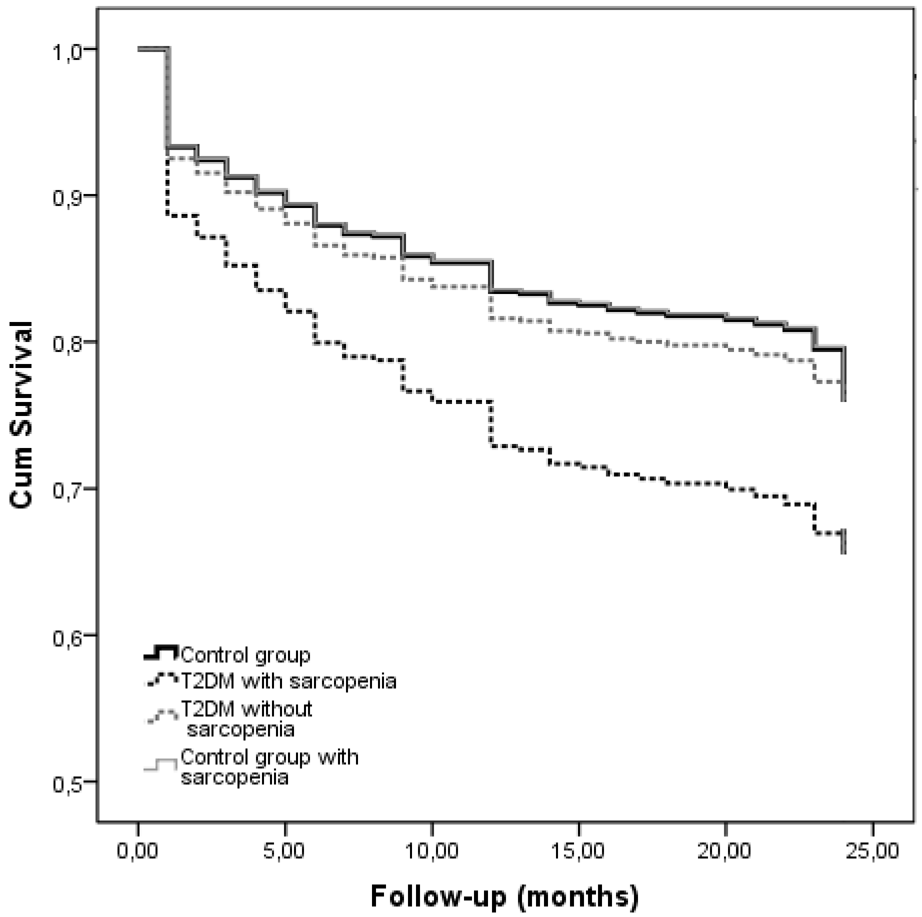
Data expressed as mean ± SD; median (Interquartile Range) or n (%). T2D: type 2 diabetes; IADL: instrumental activities of daily living;BMI: body mass índex; HS: handgrip strength;

Table 2. Cox Regression between the coexistence of sarcopenia and T2D with mortality post discharge.

	Univariate Model		Model 1		Model 2		Model 3	
	HR	**IC95%**	**HR**	**IC95%**	**HR**	**IC95%**	**HR**	**IC95%**
T2D with sarcopenia	1,61	1,08-2,35	2,88	1,15-5,15	2,04	1,06-4,48	4,03	1,25-12,94
T2D without sarcopenia	1,07	0,71-1,63	2,41	1,41-5,86	2,01	0,93-4,35	1,56	0,34-7,25
Just Sarcopenia	0,89	0,54-1,48	1,34	0,52-3,49	1,22	0,45-3,32	1,59	0,41-6,20
Control group (without T2D and sarcopenia)	1		1		1		1	

Model 1. Adjust for age and sex; model 2: adjustment for age and sex, BMI, IADL, presence of neoplasia and Charlson index> 2; model 3: analysis that excludes overweight patients, adjusted for age and sex.

Figure 2. Relationship between the presence of sarcopenia and TD2 and mortality after hospital discharge (Log-rank: 0,032).

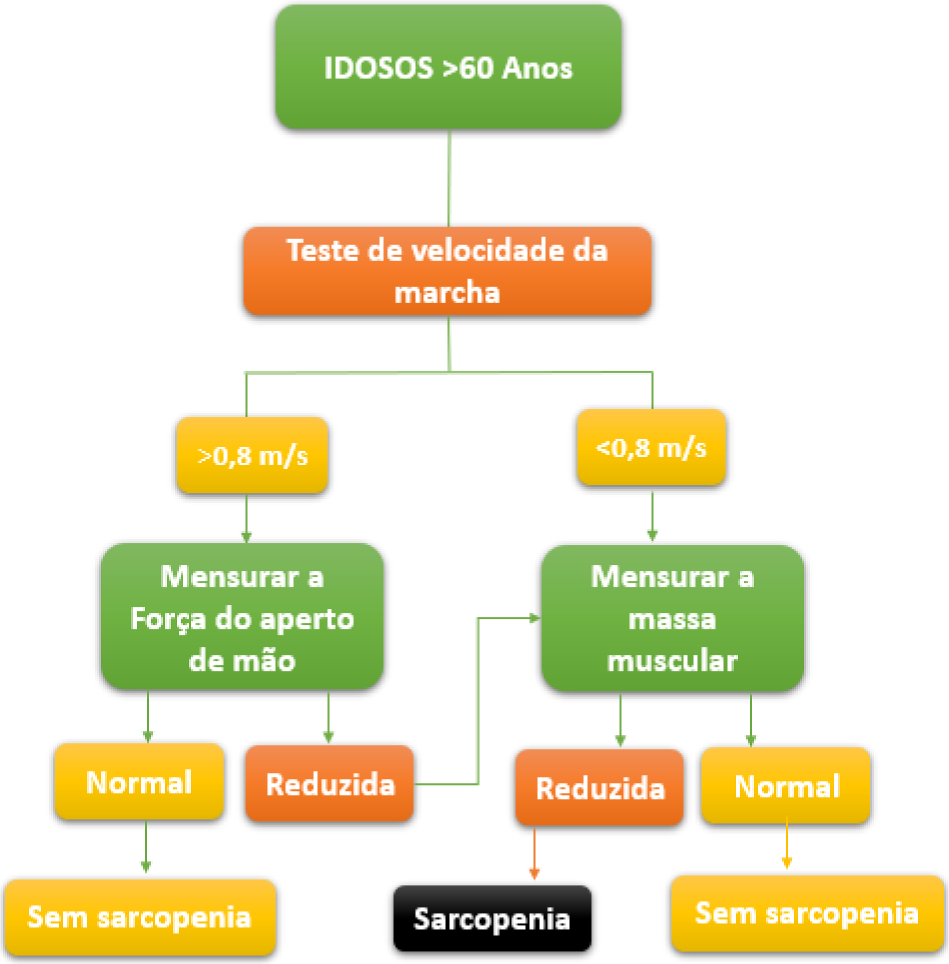


PERSPECTIVAS

As ideias apresentadas nesta tese deram apenas os seus primeiros passos no que diz respeito ao paciente idoso hospitalizado. Começamos a entender a importância que deve ser dada ao avaliar estes pacientes no contexto hospitalar e ambulatorial a fim de prevenir ou minimizar desfechos negativos. Há muitas décadas, a triagem e avaliação do paciente idoso utiliza os mesmos protocolos dos pacientes adultos. Recentemente, a força muscular passou a ser evidenciada como preditora de mortalidade nesta faixa etária além de ser incluída como um dos métodos de combate à desnutrição hospitalar em recente campanha. Diante destes fatos, espera-se uma maior atenção a estes pacientes, os quais precisam ser avaliados com protocolos específicos, incluindo a composição corporal, estado funcional e cognitivo; abordagem já realizada por médicos geriatras na avaliação geriátrica ampla, mas que passam a ter mais reconhecimento por outros profissionais devido às pesquisa e estudos recentes.

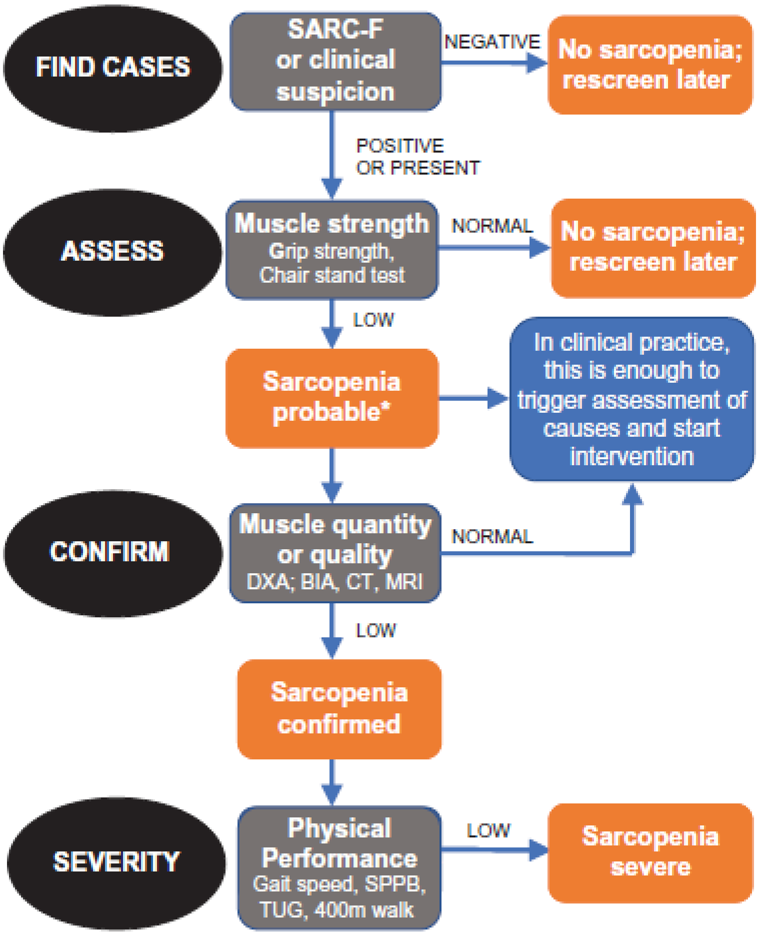
Quanto a mim, é com muito orgulho que participei deste projeto e dele fiz parte durante 4 anos. Seguirei a mesma linha de estudos e tenho como perspectiva reavaliar os pacientes dessa coorte dando continuidade ao estudo, avaliando as possíveis alterações em medidas corporais, funcionais e cognitivas após a alta hospitalar, bem como um projeto de intervenção durante a hospitalização e após a alta hospitalar.

ANEXO I



Algorítimo de avaliação da sarcopenia proposto pelo "European Working Group on Sarcopenia in Older People" (EWGSOP)

ANEXO II



Algoritmo da Sarcopenia 2019: EWGSOP2 para detecção de casos, fazer triagem e quantificar a gravidade. As etapas do algoritmo são representadas como *Find-Assess-Confirm-Gravidade ou F-A-C-S*.
* Considerar outras razões para baixa muscular força (por exemplo, depressão, distúrbios do equilíbrio, desordens vasculares).