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Escola de Enfermagem

Programa de Pós-Graduação em Nutrição e Saúde

LUCIANA DE ABREU SILVA

TERAPIA NUTRICIONAL ENTERAL E PARENTERAL EM PACIENTES HOSPITALIZADOS: ESTADO NUTRICIONAL, ADEQUAÇÃO CALÓRICA E PROTEICA E DESFECHOS CLÍNICOS

Belo Horizonte

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ATA DE NÚMERO 99 (NOVENTA E NOVE) DA SESSÃO DE ARGUIÇÃO E DEFESA DA DISSERTAÇÃO APRESENTADA PELA CANDIDATA LUCIANA DE ABREU SILVA PARA OBTENÇÃO DO TÍTULO DE MESTRE EM NUTRIÇÃO E SAÚDE.

Aos 03 (três) dias do mês de outubro de dois mil e vinte e três, às 08:00 horas, realizou-se no Auditório da Pós-Graduação (sala 432) da Escola de Enfermagem da Universidade Federal de Minas Gerais, a sessão pública para apresentação e defesa da dissertação **"TERAPIA NUTRICIONAL ENTERAL E PARENTERAL EM PACIENTES HOSPITALIZADOS: ESTADO NUTRICIONAL, ADEQUAÇÃO CALÓRICA E PROTEICA E DESFECHOS CLÍNICOS"**, da aluna ***Luciana de Abreu Silva***, candidata ao titulo de "Mestre em Nutrição e Saúde", linha de pesquisa "Nutrição Clínica e Experimental". A Comissão Examinadora foi constituída pelas professorasdoutoras Camila Kümmel Duarte, Ann Kristine Jansen e Silvia Fernandes Maurício, sob a presidência da primeira. Abrindo a sessão, a Senhora Presidente da Comissão, após dar conhecimento aos presentes do teor das Normas Regulamentares do Trabalho Final, passou a palavra à candidata para apresentação de seu trabalho. Seguiu-se a arguição pelos examinadores com a respectiva defesa da candidata. Logo após, a Comissão se reuniu sem a presença da candidata, para julgamento e expedição do seguinte resultado final:

(X) APROVADO;
( ) APROVADO COM AS MODIFICAÇÕES CONTIDAS NA FOLHA EM ANEXO;
( ) REPROVADO.

O resultado final foi comunicado publicamente à candidata pela Senhora Presidente da Comissão. Nada mais havendo a tratar, eu, Camila Kümmel Duarte, Presidente da Comissão Examinadora, lavrei a presente Ata, que depois de lida e aprovada será assinada por mim e pelos demais membros da ComissãoExaminadora.

Belo Horizonte, 03 de outubro de 2023.

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RESUMO

As estimativas da prevalência de desnutrição em adultos hospitalizados no mundo variam entre 20 e 50%. Apesar de ser um dos maiores problemas de saúde pública mundial, ainda é altamente subdiagnosticada e subtratada. A desnutrição provoca um declínio nutricional, aumentando o risco de complicações e readmissões hospitalares. Diante desse contexto, o suporte nutricional (SN) tem sido amplamente utilizado como estratégia para prevenir e tratar a desnutrição e outras condições clínicas. Os benefícios associados ao SN são diversos, entretanto essa prática não é isenta de problemas, e compreender suas complicações é vital para atingir as demandas, mantendo a segurança e eficácia da terapia. Este estudo objetivou avaliar a prática da terapia nutricional enteral e parenteral, o estado nutricional, a adequação do aporte calórico e proteico e desfechos clínicos de pacientes internados em uso de SN. Trata-se de um estudo observacional prospectivo com dados secundários obtidos do prontuário eletrônico de pacientes internados no Hospital das Clínicas da UFMG no período de 14 de dezembro de 2021 a 14 de maio de 2023. Todas as avaliações nutricionais foram realizadas pelos nutricionistas do hospital e os dados foram coletados em fichas eletrônicas e posteriormente analisados no software SPSS. Os dados de 300 pacientes em uso de SN foram incluídos. A mediana da idade foi de 61,0 (49,0 - 69,75) anos, em relação ao estado nutricional 39,5% apresentavam desnutrição grave, segundo a avaliação contida nos prontuários. Na análise da variação da massa muscular durante a internação, mensurada a partir de equações de estimativa com dados antropométricos, três das quatro equações indicaram redução significativa ($p=0,016$, $p=0,014$ e $p=0,006$). Análises de regressão mostraram que uma maior ingestão proteica pode aumentar o tecido mole magro ($p = 0,036$). Além disso, quanto maior o número de infecções ($r=0,085$; $p=0,039$), maior a chance de estar no grupo em que houve perda de massa muscular. Em relação à adequação da ingestão , a mediana foi de 75,8% (58,0-87,0) para adequação calórica e 71,6% (51,2–86,9) para adequação proteica. Já a mediana de calorias por kg de peso corporal foi de 20,0 kcal (15,7–24,4), e a ingestão mediana de proteínas por kg foi de 1,0 grama (0,9–1,2). A taxa de mortalidade foi de 30,3% e pacientes com maior infusão calórica e proteica, foram associados a um maior tempo de internação, sendo a maior ingestão proteica por kg, protetora para o óbito e foi preditora do risco de encaminhamento para tratamento intensivo ($p=0,014$). Por fim, observou-se que 83,3% dos pacientes iniciaram SN em mais de 48 horas e 71,7% dos pacientes tiveram a dieta interrompida em algum momento da internação. O início tardio do SN foi associado a maior mortalidade, maior tempo de internação e menor risco de síndrome de realimentação ($p<0,001$). As interrupções esperadas foram associadas a piores resultados. Os achados deste estudo evidenciam a associação de problemas na administração do SN com os piores desfechos clínicos e declínio do estado nutricional.

Palavras-chave: Desnutrição Hospitalar. Suporte Nutricional. Massa Muscular. Adequação da ingestão. Complicações. Interrupções da dieta.

ABSTRACT

Estimates of the prevalence of malnutrition in hospitalized adults around the world vary between 20 and 50%. Despite being one of the biggest public health problems in the world, it is still highly underdiagnosed and undertreated. Malnutrition causes nutritional decline, increasing the risk of complications and hospital readmissions. Given this context, nutritional support (NS) has been widely used as a strategy to prevent and treat malnutrition and other clinical conditions. The benefits associated with NS are diverse, however this practice is not without problems, and understanding its complications is vital to meet the demands, maintaining the safety and effectiveness of the therapy. This study aimed to evaluate the practice of enteral and parenteral nutritional therapy, nutritional status, adequacy of caloric and protein intake and clinical outcomes of hospitalized patients using NS. This is a prospective observational study with secondary data obtained from the electronic medical records of patients admitted to the Hospital das Clínicas of UFMG from December 14, 2021 to May 14, 2023. All nutritional assessments were carried out by the hospital's nutritionists and data were collected in electronic forms and later analyzed using SPSS software. Data from 300 patients using NS were included. The median age was 61.0 (49.0 - 69.75) years, in relation to nutritional status, 39.5% were severely malnourished, according to the assessment contained in the medical records. In the analysis of the variation in muscle mass during hospitalization, measured using estimation equations with anthropometric data, three of the four equations indicated a significant reduction ($p=0.016$, $p=0.014$ and $p=0.006$). Regression analyzes showed that higher protein intake can increase lean soft tissue ($p = 0.036$). Furthermore, the greater the number of infections ($r=0.085$; $p=0.039$), the greater the chance of being in the group in which there was loss of muscle mass. Regarding adequacy of intake, the median was 75.8% (58.0-87.0) for caloric adequacy and 71.6% (51.2–86.9) for protein adequacy. The median calories per kg of body weight was 20.0 kcal (15.7–24.4), and the median protein intake per kg was 1.0 grams (0.9–1.2). The mortality rate was 30.3% and patients with higher caloric and protein infusion were associated with a longer length of stay, with higher protein intake per kg being protective for death and was a predictor of the risk of referral to intensive treatment. ($p=0.014$). Finally, it was observed that 83.3% of patients started NS after more than 48 hours and 71.7% of patients had their diet interrupted at some point during hospitalization. Late onset of NS was associated with higher mortality, longer hospital stay and lower risk of refeeding syndrome ($p<0.001$). Expected interruptions were associated with worse outcomes. The findings of this study highlight the association of problems in the administration of NS with worse clinical outcomes and decline in nutritional status.

Keywords: Hospital Malnutrition. Nutritional Support. Muscle mass. Adequacy of intake. Complications. Diet interruptions.

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LISTA DE ABREVIATURAS E SIGLAS

ANVISA	Agência Nacional de Vigilância Sanitária
ALM	Appendicular Lean Mass
ASPEN	*American Society for Parenteral and Enteral Nutrition*
BIA	Análise de Bioimpedância
BW	Body Weight
CAAE	Certificado De Apresentação E Apreciação Ética
CB	Circunferência Do Braço
CC	Calf Circumference
CP	Circunferência Da Panturrilha
DEXA	Absorciometria de raios-x de dupla energia
DXA	Dual-energy X-ray absorptiometry
EFFORT	The Effect of Higher Protein Dosing in Critically Ill Patients
EMTN	Equipes Multidisciplinares de Terapia Nutricional
ESPEN	*European Society of Parenteral and Enteral Nutrition*
FFM	Fat Free Mass
G	Gender
GET	Gasto Energético Total
GER	Gasto Energético em Repouso
GLIM	Global Leadership Initiative on Malnutrition
Ht	Height
IMC	Índice de Massa Corporal
LOS	Length of Hospital Stay
LOSNS	Length of Hospital Stay Using Nutritional Support
LST	Lean Soft Tissue
M	Male

MAC	Mid-Arm Circumference
MG	Minas Gerais
MRI	Magnetic Resonance Imaging
NE	Nutrição Enteral
NP	Nutrição Parenteral
SCCM	Society of Critical Care Medicine
SEE	Standard Error of The Estimate
SMM	Skeletal Muscle Mass
SN	Suporte Nutricional
SVO	Suplementação da Via Oral
TCLE	Termo de Consentimento Livre e Esclarecido
TNE	Terapia Nutricional Enteral
TNP	Terapia Nutricional Parenteral
TMB	Taxa Metabólica Basal
UFMG	Universidade Federal de Minas Gerais
UTI	Unidade de Terapia Intensiva
W	Women

LISTA DE SÍMBOLOS

–	Menos
%	Percentual / Por cento
≤	Menor ou igual
≥	Maior ou igual
β	Coeficiente Beta
cm	Centímetros
DP	Desvio padrão
g	Gramas
g/Kg/dia	Gramas por Quilo por dia
h	Horas
IC 95%	Intervalo de Confiança 95%
IQ	Intervalo interquartil
Kcal	Quilocalorias
Kcal/Kg/dia	Quilocalorias por Quilo por dia
Kg	Quilogramas
M	Metros
N	Tamanho da amostra de estudo / número de itens/pacientes
nº	Número
p	Valor de p
P25	Percentil 25
P75	Percentil 75
Δ%	Variação percentual
r^2	Coefficient of determination
vs	Versus

APRESENTAÇÃO

A presente dissertação intitulada "**TERAPIA NUTRICIONAL ENTERAL E PARENTERAL EM PACIENTES HOSPITALIZADOS: ESTADO NUTRICIONAL, ADEQUAÇÃO CALÓRICA E PROTEICA E DESFECHOS CLÍNICOS**" é composta pelas seções "Introdução", "Justificativa" "Objetivos", "Métodos", "Resultados e Discussão", "Considerações Finais", "Referências Bibliográficas", "Apêndices" e "Anexos". A seção "Resultados e Discussão" é composta por três artigos originais redigidos de acordo com as normas de formatação das revistas a qual serão submetidas. As referências encontram-se expressas no estilo Vancouver. A estrutura desta dissertação atende aos requisitos exigidos na Resolução 10/2017, de 10 de agosto de 2017, do Colegiado de Pós-graduação em Nutrição e Saúde da Escola de Enfermagem da Universidade Federal de Minas Gerais (UFMG).

SUMÁRIO

1. INTRODUÇÃO

1.1. Desnutrição Hospitalar

Em condições normais, o ser humano é capaz de suprir suas necessidades nutricionais por meio da alimentação por via oral. Contudo, diversas situações, como a hospitalização, o tempo de permanência hospitalar e até mesmo as doenças, podem levar a alterações dessa capacidade e, consequentemente, ao comprometimento do estado nutricional e da evolução clínica dos pacientes. Tais situações devem ser identificadas efetivamente para que esse quadro seja revertido de modo eficiente, garantindo a segurança do paciente (1).

O termo desnutrição, era utilizado há pelo menos 6 anos atrás, de forma ampla, para descrever os desequilíbrios na nutrição. Recentemente, uma definição de desnutrição foi proposta pela *European Society of Parenteral and Enteral Nutrition* (ESPEN), como o estado resultante da deficiência de nutrientes, que leva a alterações na composição corporal, ocasionando redução da funcionalidade física e mental com comprometimento no quadro clínico da doença (2).

As estimativas da prevalência de desnutrição em adultos hospitalizados no mundo, variam entre 20 e 50%, sendo que 40 a 60% estão presentes no momento da admissão hospitalar em países latino-americanos (3). Estima-se que dois terços dos pacientes internados com desnutrição na admissão, se não forem tratados, irão evoluir para um maior comprometimento nutricional, afetando adversamente sua recuperação e aumentando o risco de complicações e readmissões hospitalares (4).

Apesar de se tratar de um dos maiores problemas de saúde pública mundial, a desnutrição hospitalar ainda é altamente subdiagnosticada e subtratada (5). Principalmente, devido à existência de diferentes métodos para diagnóstico, populações bem heterogêneas, além de períodos distintos de tempo de internação, que contribuem para a discrepância de dados referentes à prevalência da desnutrição no contexto hospitalar (6). Desta forma, a Global Leadership Initiative on Malnutrition (GLIM) construiu um consenso global em torno dos principais critérios diagnósticos para desnutrição em adultos em ambientes clínicos (2). O consenso propôs que, para o diagnóstico de desnutrição, é necessário pelo menos um critério fenotípico (perda de peso não intencional, baixo índice de massa corporal ou massa muscular reduzida)

e um critério etiológico (ingestão alimentar reduzida ou má absorção, ou inflamação) (2).

Durante a hospitalização, os grupos que apresentam maior risco de desnutrição são pacientes idosos, críticos e cirúrgicos (3). A população idosa também apresenta maior prevalência de sarcopenia e caquexia (7). A caquexia caracteriza-se por uma síndrome multifatorial complexa, associada à doença subjacente, com perda de peso, perda de massa muscular com ou sem perda de massa gorda, onde ocorre um catabolismo proteico intenso (8). Já a sarcopenia é uma doença muscular caracterizada pela baixa força muscular como parâmetro primário, seguida da baixa massa muscular (9). Segundo as diretrizes revisadas, a força muscular precede a massa devido ao seu papel mais relevante na previsão de resultados adversos em relação à redução da função (9). Portanto, os pacientes hospitalizados geralmente podem cursar com a desnutrição combinada de caquexia e/ou sarcopenia, em oposição à desnutrição isoladamente, aumentando ainda mais os prejuízos (10). Destaca-se que há uma falta de padronização destes termos na prática clínica e isso interfere na identificação imediata do diagnóstico e tratamento (9).

Estudos demonstram que pacientes com diagnóstico de desnutrição apresentam menor força muscular, por esse processo reduzir a síntese proteica, culminando em atrofia das fibras musculares e redução da massa muscular e funcionalidade (11). O estudo EMPOWER, uma coorte observacional e prospectiva, avaliou 378 pacientes idosos hospitalizados com 70 anos ou mais, e demonstrou que um alto risco de desnutrição foi associado à menor massa muscular (12). Além disso, o estudo de Pourhassan (13), com 41 idosos frágeis, concluiu que a desnutrição pelos critérios GLIM foi associada à perda de massa muscular durante a hospitalização de 2 semanas. Esses achados reforçam a suposição de que pacientes desnutridos perderiam mais massa muscular durante o repouso no leito, comparados àqueles eutróficos.

1.2. Massa Muscular

Os músculos atuam mantendo a homeostase glicêmica, sendo o principal tecido para sua captação de glicose no sangue, estimulada pela insulina (14). Também participam do armazenamento e utilização de substratos do metabolismo energético, como ácidos graxos e aminoácidos, além da síntese de glicogênio e termorregulação (15). Ainda, secretam miocinas que exercem funções de regulação do seu metabolismo

próprio e de outros órgãos e tecidos, dentre eles os ossos, tecido adiposo, fígado, pâncreas e o cérebro (16).

O avanço da idade é fator preditor da redução do músculo esquelético, como consequência de inatividade física e desuso (15), porém as últimas também acontecem em ambiente hospitalar. Mais precisamente em pacientes hospitalizados, a redução da força e massa muscular se dão pela associação desses fatores à doença, baixa deambulação, infecção, estresse oxidativo e hospitalizações agudas (17). Uma revisão mostrou que pacientes hospitalizados passam entre 87 e 100% do tempo deitados na cama ou sentados,com os pacientes na UTI apresentando o nível mais alto de inatividade, independentemente do motivo da internação (18). Os baixos níveis de atividade física associam-se a piores resultados na saúde, como o aumento do tempo de internação e maior risco de reinternação, além de maior declínio funcional e mortalidade (19,20,21).

A interrupção na regulação do turnover proteico do músculo esquelético ocasiona desequilíbrio dos processos catabólicos e anabólicos, sendo estes os principais causadores da perda muscular induzida pelo desuso (12). Além dos fatores citados, os componentes fisiológicos contribuem para a redução da qualidade e quantidade muscular, principalmente as alterações na estrutura e composição do músculo esquelético. Assim, com o envelhecimento, ocorrem modificações nas fibras, bem como um aumento na infiltração de gordura no músculo esquelético, além da redução da força (15).

A perda muscular impacta negativamente os indivíduos, ao prolongar o tempo de recuperação e gerar incapacidade de realização de atividades diárias. Dada a carga social e os custos associados à atrofia muscular, se faz essencial a adoção de medidas para o seu tratamento e prevenção. Duas estratégias já amplamente estudadas e que se mostraram viáveis e úteis são os exercícios físicos e aporte nutricional adequado (22). Intervenções fisioterapêuticas mostram-se úteis para promover a mobilidade e a atividade física de pacientes hospitalizados. Assim, são cada vez mais prescritas e implementadas desde o início da doença crítica até a alta hospitalar (18,21).

1.2.1. Estimativa da Massa Muscular

A composição corporal é uma ciência que considera a proporção dos diferentes compartimentos corporais e sua relação com a saúde e doença (23). A mensuração da massa muscular pode ser realizada por diferentes técnicas e métodos. Quantidade muscular pode ser relatada como massa muscular esquelética corporal total, massa muscular esquelética apendicular, massa corporal livre de gordura, tecidos moles magros ou até mesmo como área transversal muscular de locais ou frações musculares específicas do corpo (9).

A massa corporal magra apendicular é definida como a soma da massa magra nos braços e pernas do indivíduo. Não inclui a massa magra do tronco, portanto exclui as vísceras e é amplamente utilizada no estudo da sarcopenia (24). Bani e colaboradores (25) avaliaram dados retrospectivos de 260 participantes objetivando buscar associações entre baixa massa muscular apendicular da coxa com a função e equilíbrio em idosos com risco de quedas. Os principais achados deste estudo foram que a massa apendicular da coxa corrigida para o Índice de massa corporal (IMC) se correlacionou fortemente aos parâmetros de equilíbrio e desempenho físico, ressaltando que a baixa massa muscular e falta de equilíbrio pode depender das regiões onde a perda muscular é mais significativa (25). A falta de equilíbrio e o baixo desempenho físico são fatores que podem alongar a permanência de indivíduos em leitos, impactando em tempo total de internação hospitalar (26).

Já a massa corporal livre de gordura, se diferencia da massa muscular esquelética por incluir outros componentes além dos músculos esqueléticos, como a água corporal, ossos, pele, órgãos, tecido conjuntivo e o componente isento de gordura das células adiposas (27). É utilizada em estudos como substituta da massa esquelética, entretanto, nem sempre é viável tal utilização, visto que, por considerar a parte não lipídica das células adiposas em sua fração, torna-se um indicador inapropriado de massa muscular esquelética em indivíduos com maior quantidade de gordura corporal (27). A proporção de massa gorda para massa livre de gordura é associada à doença hepática e distúrbios cardiometabólicos, além de piores resultados adversos, mediados por componentes de regulação do metabolismo muscular, ósseo e de gordura como as miocinas, osteocinas e adipocinas (28). Um estudo agrupou dados de 7 coortes prospectivas com 16.155 indivíduos e as análises mostraram que houve associação da massa gorda em forma de J com mortalidade

(P< 0,001; P para não linearidade = 0,003), isso significa que pacientes com maior nível de massa gorda tiveram um aumento de 50% no risco de mortalidade, enquanto para os pacientes com maior nível de massa livre de gordura, houve redução de 30% no risco de mortalidade. Os achados reforçam que a composição corporal é um fator de prognóstico do risco de mortalidade, a massa gorda e a massa livre de gordura atuam de forma oposta. Estando o excesso de massa gorda relacionado ao aumento do risco, enquanto a massa livre de gordura protege contra o risco de mortalidade (29).

Os tecidos moles magros são a soma da água corporal, carboidratos, lipídios não gordurosos, proteína corporal total e minerais dos tecidos moles. Logo, são excluídos os compartimentos minerais de ossos e gordura, sendo a massa muscular esquelética um componente essencial dessa fração (23). Ao nível de diferenciação, se não for possível mensurar a massa/ densidade óssea, esta deverá ser calculada com a massa muscular esquelética e se obterá a massa livre de gordura. Por outro lado, se for possível mensurá-la, ao separá-la da massa esquelética obtêm-se tecido mole magro e massa óssea. Com isso, a metodologia utilizada para cada análise é o que diferencia a fração analisada (30). Cabe ressaltar que existe uma dificuldade na identificação e mensuração da massa muscular devido à complexidade da escolha das variáveis a serem medidas, definição dos pontos de corte e equipamentos de precisão. Esta realidade afeta a forma de realização dos estudos e prejudica o entendimento, limitando a capacidade de comparações individuais e avaliação das intervenções terapêuticas (9).

1.2.2. Métodos de Avaliação e Mensuração da Massa Muscular

Já é consenso que as medidas mais simplificadas de avaliação corporal, como o peso e o índice de massa corporal, apesar de úteis e bem conhecidas, são pouco sensíveis a grupos específicos como os pacientes com obesidade ou em determinadas condições clínicas de saúde. Com o passar dos anos, juntamente ao avanço tecnológico, surgiram técnicas para estimar a composição corporal usando diferentes ferramentas. Principalmente em relação à massa muscular, os dados antropométricos e instrumentos de imagem destacam a importância das variadas frações de massas musculares e seus parâmetros associados, sendo fundamental nas decisões de prevenção, diagnóstico e tratamento (23).

Dentre as diferentes modalidades utilizadas para estimativa da massa muscular, estão: antropometria, análise de bioimpedância (BIA), absorciometria de raios-x de dupla energia (DEXA), ressonância magnética, tomografia computadorizada e ultrassom.

A antropometria compreende o estudo das medidas e proporções corporais, desde comprimentos e larguras, circunferências até espessuras de dobras cutâneas do corpo humano, mediante ferramentas como balanças, fitas e adipômetros. Trata-se de um método objetivo, barato, não invasivo, de fácil realização e facilmente aplicável em grandes populações de estudos. Entretanto, as medidas sozinhas são pouco específicas para determinar a massa muscular. Podem ocorrer variações entre os avaliadores, além de, em pacientes com distúrbios hidroeletrolíticos, pode haver superestimação pela presença de edemas e interpretação inadequada dos dados (31).

A BIA é uma opção para a estimativa de massa apendicular e total. O equipamento não mensura diretamente a massa muscular, mas a estima juntamente com o volume de gordura baseada na condutividade elétrica pelo corpo relacionada à água e à distribuição iônica (9). Nesse princípio, a massa livre de gordura, composta por água e eletrólitos, apresenta maior condutividade do que os tecidos gordurosos, permitindo a estimativa da composição corporal (32). Configura-se como uma ferramenta portátil, acessível e reprodutível, no entanto, necessita de equações de populações pré-estabelecidas, podendo haver discrepâncias para sua utilização na prática clínica. Ademais, o estado de hidratação do paciente e as variedades de equipamentos podem influenciar nas medições, superestimando a massa muscular e subestimando a massa gorda (33).

A tomografia computadorizada e a ressonância magnética são consideradas padrão-ouro para avaliação da massa muscular (33). No entanto, apresentam limitações devido ao alto custo e necessidade de avaliador treinado, sendo limitados em ambientes de atenção primária. Além de não possuírem pontos de corte bem delimitados a essas medidas, a dose de radiação é considerável, não sendo indicados para medições repetidas (9,23)

DEXA é o instrumento mais utilizado para determinar a massa muscular. Consiste na propriedade dos raios-x de produzirem imagens internas de onde o feixe de uma pequena dose de radiação passa no corpo. O tecido adiposo e o músculo

esquelético compreendem principalmente água e compostos orgânicos, que restringem menos o fluxo de raios-x do que o osso (31,34). Dentre as suas vantagens, fornece uma estimativa segura e reprodutível para medidas repetidas de massa muscular, possui rápida aplicação e pontos de corte estabelecidos. Suas desvantagens envolvem o fato de não ser portátil, influência do estado de hidratação do paciente e sua precisão pode variar em pessoas de diferentes idades e diferentes condições patológicas (33).

O ultrassom detém a capacidade de quantificar a espessura do tecido, sendo viável na clínica para diagnóstico e acompanhamento por fornecer resultados mais qualitativos do que quantitativos. Trata-se de uma técnica simples, segura e de baixo custo, apesar disso, a medição muscular é mais propensa a erros técnicos ocasionados por fatores como posicionamento, falta de técnica, hidratação, capacidade de garantir um estado de relaxamento ou contração total do músculo (23).

Diante de todas as vantagens e desvantagens de cada método apresentado, ressalta-se o achado do estudo de Bruyère et al. (35) que evidenciou que a ferramenta mais utilizada na prática clínica foi a antropometria (dados antropométricos, como a circunferência da panturrilha), seguida do DEXA (57,5% e 45,9%, respectivamente). Existe uma gama de medidas antropométricas e cada uma possui peculiaridades, refletem o estado nutricional e ajudam a estimar o prognóstico clínico. Estudos sugerem que um ajuste dos dados antropométricos para sexo, IMC e idade resulta em uma melhor correlação com a massa magra medida por DEXA (33). Ressalta-se que a antropometria ajustada é uma alternativa viável e barata, mas necessita de adaptações e combinações de dados específicos para a população avaliada, para garantir maior acurácia e minimizar os erros de predição.

1.3. Necessidades Nutricionais

Em pacientes com condições de saúde específicas, como doenças em estágio avançado, idosos e pacientes críticos, debilidades no estado nutricional podem prejudicar o desempenho, a qualidade de vida e a sobrevida. Portanto, pacientes com ingestão oral diminuída necessitam de intervenção nutricional para manter o estado nutricional e atender às necessidades energéticas e proteicas (36).

Quando a ingestão é igual ao gasto de energia, o corpo está em balanço energético e há uma manutenção do peso corporal (37,38). Quando a ingestão excede o gasto energético, ocorre um estado de balanço energético positivo e a consequência é um aumento na massa corporal, dos quais 60 a 80% é geralmente gordura corporal (38). Por outro lado, quando o gasto de energia excede a ingestão de energia, ocorre um estado de balanço energético negativo e a consequência é uma perda de massa corporal (38). O balanço energético é controlado por sinais neuroendócrinos, portanto, há um controle rigoroso fisiológico, ao mesmo tempo, em que é influenciado por fatores internos e externos que interferem no processo (39).

O gasto energético é um ponto de referência essencial para o estabelecimento da melhor terapia nutricional e, em condições normais, recomenda-se que a oferta de energia seja igual ao gasto para evitar oscilações da composição corporal (40). Entretanto, existem condições clínicas nas quais o gasto energético total (GET) está alterado devido a diversos fatores como as patologias que induzem alterações metabólicas, catabolismo intenso, dor e infecções e podem aumentar o gasto energético em repouso (GER). Além da desnutrição e comprometimento da condição clínica, que podem reduzir o GER (40).

A desnutrição é reflexo de um balanço energético negativo, que pode surgir de uma ingestão reduzida de energia, um maior gasto energético ou uma combinação de ambos (41).

Nesses casos, quando a disponibilidade de energia é menor do que o GER, os sistemas fisiológicos do corpo se ajustam, promovendo a conservação de energia para funções essenciais, como manutenção celular, termorregulação e locomoção (42). Assim, há uma supressão da taxa metabólica basal (TMB), e os processos não essenciais para a sobrevivência a curto prazo, como a renovação óssea, são interrompidos (42).

Na desnutrição recomenda-se que a ingestão energética seja superior ao gasto para as reservas endógenas serem repostas (40). Portanto, as necessidades proteicas também estão aumentadas para manter um balanço positivo de nitrogênio (43) e estudos mostraram que o fornecimento precoce de energia de até 70% a 80% do gasto energético está associado a melhores resultados nos estágios iniciais do catabolismo em pacientes graves (44).

O balanço de nitrogênio é determinado a partir da comparação da quantidade de nitrogênio ingerida com a quantidade excretada pela urina. Um saldo negativo indica catabolismo proteico, e o balanço positivo indica um estado anabólico (45). O catabolismo proteico, pode resultar na ativação excessiva da via ubiquitina-proteassoma, que causa depleção de aminoácidos essenciais para a reparação celular ou tecidual e, portanto, pode gerar o aumento na síntese de mediadores inflamatórios, declínio da massa muscular esquelética e disfunção metabólica a longo prazo (45,46).

Em contraste, a ingestão adequada de proteínas ativa os processos anabólicos que diminuem a inflamação, atenuam os danos aos tecidos e melhoram a função imunológica (45). Contudo, apesar de ser valioso no monitoramento da ingestão, na prática clínica, o uso do balanço nitrogenado apresenta limitações como a influência da dieta, estado de hidratação, doenças renais; perdas de nitrogênio em decorrência de diarreia e fístulas além da imprecisão da coleta das amostras (47).

Existem vários métodos para a determinação das necessidades energéticas, sendo a calorimetria indireta considerada o “padrão ouro” na determinação do gasto energético de repouso (48). Trata-se de um método não invasivo com alta precisão, porém, devido ao seu alto custo, baixa disponibilidade dos equipamentos e a necessidade de pessoal treinado para realizar a medição, sua aplicação é limitada e restrita a poucas instituições (49).

Assim, na ausência da calorimetria, as fórmulas de bolso e equações preditivas para estimativa do gasto energético são frequentemente utilizadas na prática clínica (49). Apesar de muito utilizadas, as equações apresentam limitações, visto que foram comumente desenvolvidas em populações saudáveis e, portanto, não atendem com eficácia a casos específicos como os pacientes críticos e idosos (48,49). A determinação precisa das necessidades nutricionais é importante para fornecer o aporte adequado de nutrientes, prevenindo assim a desnutrição hospitalar, infecções, e reduzir o tempo de internação hospitalar e mortalidade (49).

1.4. Suporte Nutricional

O Suporte Nutricional (SN) é definido como um conjunto de procedimentos que visa manter ou recuperar o estado nutricional do paciente, por meio de suplementação da via oral (SVO), Nutrição Enteral (NE) e/ou Parenteral (NP) (50,51), garantindo o aporte adequado de nutrientes (52). Conforme a definição estabelecida pela ESPEN (53), o

suporte nutricional compreende desde a fortificação de alimentos e suplementação da via oral, até a NE (via sonda) e NP. Seu principal objetivo é nutrir o paciente por vias alternativas, visando o aumento da ingestão de calorias, advindas dos macronutrientes e/ou micronutrientes.

Essa modalidade terapêutica é regulamentada no Brasil, devendo ser realizada pelas Equipes Multidisciplinares de Terapia Nutricional (EMTN), ao nível hospitalar. Está indicada quando existe um risco nutricional iminente e em situações de impossibilidade na utilização da via oral com ingestão alimentar oral insuficiente (inferior a 60% das recomendações) no período de 3 a 5 dias consecutivos, sem expectativa de melhora da ingestão. Deve ser mantida até que o paciente seja capaz de consumir 75% de suas necessidades nutricionais pela via oral (54).

As EMTN são responsáveis pelo fornecimento do SN e são constituídas por profissionais de todos os seguimentos da equipe de saúde (médico, enfermeiro, nutricionista, farmacêutico); outros profissionais relevantes como fisioterapeutas e fonoaudiólogos também podem fazer parte da equipe. O principal objetivo desse grupo é apoiar a equipe hospitalar no fornecimento do SN, para garantir que as necessidades nutricionais dos pacientes sejam atendidas, especialmente para aqueles que necessitam de NE ou NP (55). Atuam em conjunto visando prover uma nutrição otimizada aos pacientes, além de normatizar os procedimentos e registros relativos ao SN, zelando pela sua prática adequada e maior segurança (54).

O SN é fundamental para redução da morbimortalidade hospitalar, contribuindo para prevenir e tratar a desnutrição, concomitantemente, melhorar os desfechos clínicos, reduzindo o tempo de internação e consequentemente os custos associados (54,56). Além disso, o uso do SN pode auxiliar na redução da inflamação, na melhora da resposta imunológica e na modulação da resposta metabólica ao trauma, além de preparar o paciente para o procedimento cirúrgico e clínico, prevenir e tratar as complicações decorrentes do tratamento e da doença, bem como melhorar a qualidade de vida do paciente (57,58).

A determinação do tipo de SN a ser instituído dependerá de um conjunto de fatores, dentre eles: doença de base, idade, quadro clínico do paciente, avaliação nutricional e risco nutricional, capacidade digestiva-absortiva do trato gastrintestinal, necessidade nutricional, possibilidade de ingestão oral, hábitos alimentares e o custo (59).

Os benefícios associados ao SN são diversos. Estudos mais recentes como o EFFORT (60), realizado na Suíça com mais de 2.000 pacientes hospitalizados, demonstrou que o SN foi eficaz para reduzir os riscos de complicações e mortalidade e ainda melhorar os resultados funcionais. Já em outro estudo de coorte com 69.934 pacientes desnutridos, a taxa de mortalidade intra-hospitalar foi significativamente menor entre os pacientes que receberam SN em comparação com aqueles que não receberam (7,2% vs 8,8%, respectivamente, $p<0,001$); o mesmo ocorreu para a taxa de reinternação hospitalar que foi menor no grupo que recebeu SN (18,3% vs 19,1%, $p = 0,002$) (61).

1.4.1. Terapia Nutricional Enteral

Entende-se por terapia nutricional enteral (TNE) o conjunto de procedimentos terapêuticos empregados para recuperação e/ou manutenção do estado nutricional por meio de nutrição enteral (53). Segundo a RDC n.° 63 da Agência Nacional de Vigilância Sanitária (ANVISA) (51), a TNE pode ser definida de forma mais abrangente como: “alimento para fins especiais, com ingestão controlada de nutrientes, na forma isolada ou combinada, de composição definida ou estimada, especialmente formulada e elaborada para uso por sondas ou via oral em pacientes desnutridos ou não, conforme suas necessidades nutricionais, em regime hospitalar, ambulatorial ou domiciliar, visando a síntese ou manutenção dos tecidos, órgãos ou sistemas”.

A TNE e a terapia nutricional parenteral (TNP) possibilitam que o paciente atinja as suas necessidades calóricas e proteicas, no entanto, existem indicações específicas para cada uma delas. A TNE deve ser considerada primeiro sempre que o trato gastrointestinal estiver funcionante, seja total ou parcialmente e a nutrição oral permanecer inadequada (insuficiente para atingir 60% das necessidades nutricionais diárias), apesar das intervenções nutricionais (36).

De acordo com o preconizado pelas diretrizes da ESPEN, a TNE só deverá ser instituída quando houver necessidade de utilizá-la por pelo no mínimo 5 a 7 dias, podendo ser associada a via oral ou a TNP, quando não se consegue alcançar 60% das necessidades calóricas por uma via isolada (62). Além disso, existem benefícios ao se empregar a TNE, pois esta reduz a translocação bacteriana, auxilia na manutenção da microbiota intestinal, reduz o nível das citocinas inflamatórias circulantes, apresenta maior custo-benefício e está associada a menor risco de complicações que a TNP (59,63).

Em relação às formulações, as fórmulas enterais padrão são nutricionalmente completas e caracterizam-se por apresentar uma composição que atende às necessidades nutricionais da população em geral. Em comparação, as fórmulas enterais específicas para doenças são desenvolvidas para atender às demandas nutricionais e metabólicas específicas, por exemplo, para pacientes com câncer, insuficiência renal, diabetes, úlceras por pressão, doença pulmonar e cirrose (55). As fórmulas são definidas de acordo com vários fatores, desde a sua complexidade até a sua composição. Podem ser classificadas em poliméricas, oligoméricas ou elementares, segundo o grau de hidrólise e absorção dos macronutrientes (64,65).

Nos últimos anos, foi estabelecido o conceito de TNE precoce, definido como a oferta de NE entre 24 e 48 horas após admissão na Unidade de Terapia Intensiva (UTI), ou seja, após um evento traumático (66). Surge com a premissa de evitar que a ausência de nutrientes no trato gastrintestinal leve a ocorrência da translocação bacteriana e sepse, que aumentam a mortalidade (57). A alimentação trófica foi desenvolvida e adotada na prática clínica como uma alternativa ao jejum enteral completo (67). Caracteriza-se por fornecer baixas doses de alimentação enteral (geralmente 10 - 30 mL/h), com intuito de nutrir minimamente o paciente, bem como permitir a transição para alimentação enteral completa independente da nutrição parenteral mais rapidamente (68,69).

Essa prática reduz potencialmente o risco de complicações sépticas, evita hiperglicemia e baixa tolerância gastrointestinal, além de minimizar o risco de superalimentação de tecidos metabolicamente ativos e consequências adversas associadas em pacientes críticos com sobrepeso e obesidade (68). Estudos sugerem que a oferta de 50% a 65% das calorias prescritas podem ser necessárias para gerar benefícios como: preservar a função da barreira intestinal, evitando aumento na permeabilidade em pacientes queimados e submetidos ao transplante, mantém a função imunológica e melhora a imunomodulação das fórmulas enterais em pacientes críticos além de prevenir complicações posteriores (69,70).

1.4.2. Terapia Nutricional Parenteral

A NP, segundo a Portaria 272 da ANVISA (50), consiste em: “solução ou emulsão, composta basicamente de carboidratos, aminoácidos, lipídios, vitaminas e minerais, estéril e apirogênica, acondicionada em recipiente de vidro ou plástico, destinada à administração intravenosa em pacientes desnutridos ou não, em regime hospitalar,

ambulatorial ou domiciliar, visando a síntese ou manutenção dos tecidos, órgãos e sistemas".

A NP é indicada para suprir as necessidades nutricionais e metabólicas de pacientes impossibilitados de fazê-la por outras vias (71). Essa indicação deve ser feita quando o trato gastrointestinal é não funcionante e inclui considerações sobre a capacidade absortiva digestiva, o tempo de uso, riscos e complicações associadas. As principais indicações em adultos para o uso da NP são a insuficiência intestinal devido à doença ou tratamento (doenças inflamatórias intestinais e síndrome do intestino curto), obstrução intestinal grave, fístulas de alto débito, ou trato gastrointestinal inativo (72).

Em caso de contraindicação para uso do SN oral ou NE, a NP deve ser implementada assim que possível em pacientes desnutridos, de forma precoce e progressiva, podendo ser fornecida em detrimento ao jejum, em caso de contraindicações para NE. A NP progressiva consiste em iniciar com um aporte de baixa densidade calórica (1.000 kcal/d ou menos) e ir aumentando gradativamente (62). Nos pacientes que apresentam risco de desnutrição, é recomendado iniciar a NP mais cedo, dentro de 3 a 6 dias, caso seja improvável que eles alcancem as necessidades pela nutrição oral. Já para pacientes bem nutridos, o início da NP (suplementar ou completa) é indicado para aqueles que não conseguem atingir as demandas nutricionais após 7 dias (72).

Quanto às fórmulas, destinam-se a fornecer calorias e nutrientes, e devido a sua administração por via intravenosa, as soluções parenterais são compostas de glicose, emulsão lipídica e aminoácidos, podendo ser acrescida de eletrólitos, vitaminas e oligoelementos conforme a necessidade (55). O mesmo fator que garante a oferta de nutrientes na NP, também é risco para complicações: o acesso venoso (72).

1.4.3. Complicações associadas ao Suporte Nutricional

O SN não é isento de problemas, e compreender suas complicações é vital para atingir as demandas, mantendo a segurança e eficácia da terapia. Dentre as suas ocorrências estão a síndrome de realimentação, definida como a ruptura grave no equilíbrio de eletrólitos, e ocorre em indivíduos desnutridos e obesos quando alimentados após períodos de privação alimentar ou quando apresentam baixas

reservas corporais. Os sintomas podem incluir alterações cardíacas, edema periférico, insuficiência respiratória, encefalopatia e outras disfunções graves (55).

A síndrome geralmente ocorre nos primeiros quatro dias após o início do SN, tem incidência de 14 a 28% e pode ser diagnosticada através da deficiência de tiamina, além de hipofosfatemia, hipomagnesemia e hipocalemia (55). Em relação a NP, a síndrome de realimentação também pode estar presente, além de outras alterações metabólicas como hiperglicemia, anormalidades na função hepática e renal (73). A hiperglicemia é a complicação mais comum da TNP, e a ausência do controle glicêmico em pacientes com parenteral tem sido associada a piores efeitos tanto em pacientes críticos quanto em não críticos. Uma alternativa viável é iniciar a TNP lentamente e monitorar os níveis de glicemia frequentemente (72).

A hiperglicemia é a comum em pacientes hospitalizados que iniciam em NP, onde 50% dos pacientes hospitalizados apresentam pelo menos um episódio durante a internação (74). Pode ser causada por vários fatores como a sepse, diabetes subjacente, excesso de infusão de carboidratos e uso de medicamentos como os esteróides (73).

Os pacientes com doenças agudas, ou submetidos a cirurgias e traumas têm maior risco de desenvolver hiperglicemia devido ao aumento da produção hepática de glicose e da resistência periférica à insulina (74). A hiperglicemia pelo excesso de infusão de dextrose ocorre quando, após a infusão da NP, há uma elevação da glicose sérica cuja secreção de insulina endógena é ajustada à taxa de infusão de dextrose (75). Quando não controlada, pode levar à disfunção do sistema imunológico, aumento das taxas de mortalidade, maior susceptibilidade às infecções e aumento do tempo de internação (74,75). Um estudo observacional retrospectivo foi realizado com 226 pacientes que receberam NP. Os resultados demonstraram que aqueles com DM2 apresentando hiper ou hipoglicemia tiveram uma mortalidade significativamente maior comparados aos não diabéticos tanto intra-hospitalar como após 6 meses de uso da NP (76).

A hipoglicemia também é comum e contribui para as altas taxas de mortalidade e complicações. As suas principais causas são a interrupção repentina do suporte nutricional, dosagem inadequada da terapia com insulina, além de falência progressiva de múltiplos órgãos (76). As interrupções da infusão do SN, tanto previstas quanto imprevistas, que acontecem principalmente pelas intervenções

médico-cirúrgicas que visam estabilizar os pacientes hospitalizados, contribuem para o desenvolvimento de desnutrição (77). Portanto, não bastam os esforços para fornecer calorias adequadas e outros nutrientes, as complicações associadas devem ser monitoradas frequentemente.

Outra complicação metabólica comum na NP é a hipercapnia advinda da superalimentação de calorias e dextrose. A superalimentação gera um aumento na produção de dióxido de carbono durante o metabolismo de carboidratos e consequentemente aumenta a carga de trabalho respiratório, resultando em comprometimento respiratório e dificuldade no desmame da ventilação mecânica (78). A superalimentação na NP também pode levar à desidratação hipertônica, azotemia e acidose metabólica. Já a infusão excessiva de carboidratos está associada à esteatose hepática pelo aumento da proporção de insulina para glucagon e deficiência de carnitina (74,78). Enquanto isso, as infusões ricas em lipídios podem causar hipertrigliceridemia e hiperlipidemia devido à diminuição da depuração lipídica (74). Por fim, complicações gastrointestinais como a atrofia intestinal e gastroparesia também pode ocorrer quando a NP é fornecida e a nutrição enteral é suspensa devido à falta de estimulação dos nutrientes luminais e resposta hormonal prejudicada (74,75).

Complicações gastrointestinais são comumente associadas à TNE. Os volumes residuais gástricos são usados para avaliar a tolerância à NE, e pesquisas demonstram que mesmo quando esses volumes estão elevados, não há correlação com aspiração, maior duração da ventilação mecânica e piores desfechos (79). Segundo as diretrizes da Sociedade Americana de Nutrição Parenteral e Enteral (ASPEN) e da Society of Critical Care Medicine (SCCM) a tolerância à NE deve ser monitorada e a TNE suspensa apenas em casos de volume residual maior que 500 mL ou vômitos e distensão abdominal associada a dor e desconforto (58).

Outra complicação gastrointestinal é a diarreia. Embora seja frequentemente atribuída à NE, a diarreia em pacientes hospitalizados pode ter muitas causas como uso de medicamentos específicos (antibióticos, alta osmolalidade da NE, presença de sorbitol na NE) e patógenos infecciosos. Em contrapartida, esses pacientes também podem cursar com a constipação, devido à mobilidade reduzida e redução da ingestão alimentar (79). Outras complicações da NP, são a disfunção e atrofia da barreira mucosa intestinal, doença hepática associada à insuficiência intestinal, incluindo

esteatose hepática , colestase e fibrose hepática, que podem se desenvolver devido à falta de nutrição do lúmen (80,81). Estudos demonstram que a falta de NE, com instituição da NP, pode alterar a composição do microbioma intestinal e enfraquecer a função da barreira epitelial, predispondo-a à translocação bacteriana, que também está associada a complicações sépticas (82).

As complicações mecânicas associadas ao SN incluem danos aos órgãos adjacentes, deslocamento do cateter e incapacidade de seu funcionamento (75). As obstruções mecânicas podem ocorrer por precipitação de fármacos e emulsões lipídicas, entretanto, na NP, a maioria é causada por um coágulo sanguíneo (73). A ocorrência de um trombo venoso relacionado ao cateter pode ser assintomática, e em outros casos pode resultar em desconforto para o paciente com inchaço e proeminência das veias (75). Em relação às complicações mecânicas da NE, a obstrução e a exteriorização/ deslocamento do cateter são as mais prevalentes. A oclusão do cateter é uma complicação subestimada e subnotificada, que ocorre em cerca de 9% a 35% dos pacientes. As principais causas para a sua ocorrência são: a administração inadequada de medicamentos, posição do paciente no momento da ingestão, uso de fórmulas ricas em fibras, má higienização ou até mesmo por verificações frequentes do volume residual gástrico (79,83).

O deslocamento do tubo de NE é uma das complicações mais comuns, com taxas de até 13%. As principais causas de deslocamento são a retirada pelo próprio paciente e a exteriorização acidental durante os cuidados gerais (84). A longo prazo, os cateteres são mal tolerados pelo paciente consciente, por provocarem uma sensação de incômodo na faringe, se tornando uma fonte de estresse psicológico, sendo a presença do tubo um sinal visível de sua doença (83). Contudo, os pacientes com estado mental alterado também podem tentar retirar os tubos de alimentação colocados por via nasal e, às vezes, conseguem fazê-lo mesmo quando contidos (79).

As infecções são as complicações mais comuns e graves da NP, inerentes tanto ao tipo de formulação e cateter selecionados para a administração (74). Os pacientes que recebem NP também podem sofrer de doenças subjacentes significativas que podem aumentar o risco de infecção. A localização do local do cateter, ambiente do paciente e tipo de infusão também influenciam o risco de infecção (75). As infecções da corrente sanguínea relacionada ao cateter estão entre as complicações mais graves e mórbidas da terapia NP. Caracteriza-se pela confirmação

laboratorial de infecção, não relacionada a uma infecção de outro local além do catéter (74). Pacientes com maior tempo de internação, insuficiência renal ou presença de neoplasia apresentaram maiores chances de desenvolver (85). Estudos mostram que as taxas de infecções de NP para pacientes hospitalizados variam de 0,38 a 4,58 por 1.000 cateteres-dia, acometendo cerca de 2 a 20% dos pacientes que recebem NP (73,86,87).

Deve-se ressaltar que as complicações associadas ao SN podem ser evitadas ou atenuadas por meio de uma maior acuidade em relação ao processo, como a seleção do cateter adequado; preparação e acompanhamento da fórmula, bem como treinamento dos profissionais e paciente sobre a terapia (74).

2. JUSTIFICATIVA

A alta prevalência de desnutrição prejudica o estado nutricional e está associada a piores desfechos, pois impacta fortemente os pacientes, aumentando o tempo de permanência no hospital, taxas de infecção, declínio funcional, maiores custos, morbidade e mortalidade (61,88). Dados recentes destacam que cerca de 5,5% a 20,9% de pacientes hospitalizados sofrem declínio no estado nutricional (89,90). Estudos relatam que a má qualidade das refeições ofertadas, falta de apetite, interrupções no fornecimento, jejum, os efeitos da doença e do tratamento, dor e dificuldade de deglutição são os principais fatores associados ao declínio do estado nutricional (91). Percebe-se que a maior parte desses, são barreiras nutricionais evitáveis e podem ser solucionadas com a priorização da nutrição no contexto do atendimento clínico e das demandas nutricionais dos pacientes.

Diante desse contexto, o SN tem sido amplamente utilizado como uma das estratégias para prevenir e tratar a desnutrição e outras condições clínicas. Embora seja considerado um procedimento seguro, existem complicações importantes associadas a essa terapêutica que devem ser consideradas e podem levar a grandes danos, com impacto substancial na morbimortalidade, impondo uma alta carga sobre os recursos de saúde (84). O fator inovador deste estudo está na sua metodologia que permite uma avaliação completa do paciente durante todo o período da internação, possibilitando compreender a relação da terapia nutricional, suas intercorrências e os desfechos clínicos em um hospital universitário do Brasil. Os resultados encontrados serão relevantes para a prática clínica considerando a realidade de um contexto de baixos recursos, onde equipamentos e materiais robustos, muitas vezes não estão disponíveis. Assim, é possível reforçar pontos cruciais do processo, sempre considerando o paciente como o foco das terapias e promovendo recursos e informações que sejam capazes de melhorar a efetividade da atuação nutricional frente aos pacientes hospitalizados.

3. OBJETIVOS

3.1. Geral

- Avaliar o estado nutricional, a adequação do aporte calórico e proteico e desfechos clínicos de pacientes internados em uso de suporte nutricional no Hospital das Clínicas da Universidade Federal de Minas Gerais.

3.2. Específicos

- Avaliar a associação entre a variação da massa muscular durante a internação com a ingestão calórica e proteica e os desfechos clínicos e nutricionais de pacientes em uso de suporte nutricional *(Artigo Original 1)*.

- Avaliar a associação do consumo e adequação de calorias e proteínas com os desfechos clínicos de pacientes internados em um hospital público de Belo Horizonte, MG *(Artigo Original 2)*.

- Avaliar a administração de suporte nutricional e seus desfechos clínicos em pacientes internados em um hospital público de Belo Horizonte *(Artigo Original 3).*

4. MÉTODOS

4.1. Delineamento

Trata-se de um estudo observacional prospectivo realizado em um único centro (Hospital das Clínicas da Universidade Federal de Minas Gerais). O estudo recebeu aprovação do Comitê de Ética da Universidade Federal de Minas Gerais (CAAE 27966620.4.0000.5149) e da Gerência de Ensino e Pesquisa da instituição. Foram levantados dados secundários obtidos do prontuário eletrônico no período de 14 de dezembro de 2021 a 14 de maio de 2023.

O HC-UFMG é administrado pela Empresa Brasileira de Serviços Hospitalares (Ebserh), sendo uma instituição pública em que todos os procedimentos são realizados gratuitamente. Este hospital está localizado na cidade de Belo Horizonte – MG, e é referência na atenção de média e alta complexidade para a população do município de Belo Horizonte e do Estado de Minas Gerais, sendo que 40% dos atendimentos são de pacientes originários do interior do Estado. Os usuários formam uma clientela universalizada, e 100% dos pacientes são provenientes do Sistema Único de Saúde.

Todos os participantes foram esclarecidos sobre todas as competências da pesquisa, riscos e objetivos. Foi utilizada uma linguagem acessível e as dúvidas foram sanadas, seguindo a ética e sigilo dos dados conforme preconizado pelas Diretrizes e Normas Regulamentadoras de Pesquisa envolvendo Seres Humanos do Conselho Nacional de Saúde (92). Todos os participantes e/ou os responsáveis que aceitaram participar do projeto, assinaram o Termo de Consentimento Livre e Esclarecido (TCLE) e somente após essa etapa, os devidos dados foram coletados.

4.2. Amostra

Os participantes deveriam atender aos seguintes critérios de inclusão no estudo: indivíduos com idade igual ou superior a 18 anos, de ambos os sexos, admitidos pela Comissão de Suporte Nutricional, que estiveram internados no hospital em uso de terapia nutricional enteral e/ou parenteral por no mínimo 24 horas, associada ou não a via oral. Ainda como critérios de inclusão, era imprescindível a assinatura do TCLE e possuir pelo menos uma avaliação nutricional durante o período em uso de suporte nutricional.

Os critérios de exclusão foram: pacientes pediátricos; gestantes; pacientes sem informação de peso aferido ou estimado, ou com apenas dados de peso corporal ideal disponíveis. Os pacientes previamente inscritos no projeto, mas que foram posteriormente readmitidos no hospital, não foram coletados novamente.

O cálculo do tamanho da amostra foi realizado baseado no estudo de Lupián-Angulo (93 para associação do uso da TN e complicações. Neste estudo foi observada uma diferença de 11 dias no tempo de internação de pacientes que receberam mais que 80% de suas necessidades energéticas comparado com os que receberam menos que 80% das suas necessidades energéticas. Baseando-se nestas diferenças, seriam necessários 78 pacientes, considerando um poder de 80% e um alfa = 0,05.

4.3. Coleta de Dados

A coleta de dados foi realizada diariamente, exceto aos finais de semana, por uma equipe de pesquisadores treinados, composta por estudantes, nutricionistas e profissionais do serviço, sob supervisão dos pesquisadores responsáveis. Para identificar os pacientes elegíveis, foi consultado o mapa de pacientes em uso de dieta enteral e parenteral gerado diariamente pela Comissão de Terapia Nutricional do hospital. Após identificação e assinatura do TCLE, os pesquisadores coletaram dados dos prontuários clínicos e eletrônicos. Não foram solicitados dados diretamente ao paciente, ao seu acompanhante ou aos profissionais que os acompanharam. As informações coletadas foram inseridas em formulário eletrônico no Google Docs® e, após preenchimento, foram computadas em um banco de dados no programa Microsoft® Excel.

Foram coletados os seguintes dados:

- **Dados demográficos:** gênero, idade, raça/cor (autorreferida), data de nascimento, localidade.
- **Dados da internação:** número de registro, data da internação, data da alta, leito, setor da internação, comorbidades clínicas, história médica pregressa, presença de neoplasia maligna, cuidados paliativos, realização de diálise e transferência para terapia intensiva.

- **Dados sobre o estado nutricional:** peso utilizado para cálculo das necessidades nutricionais, altura, IMC, presença de edemas, diagnóstico nutricional , além das prescrições nutricionais. Estes dados nutricionais foram coletados em dois momentos, na admissão no suporte nutricional e na última reavaliação ainda no período em uso de suporte. Para coleta de dados do peso e altura foram considerados apenas os dados informados, aferidos e/ou estimados.
- **Dados sobre o suporte nutricional:** tipo de suporte (enteral ou parenteral, associado a via oral ou não), tipo de fórmula da dieta recebida, adequação da infusão inicial de proteínas e calorias e consumo médio do período em suporte.
- **Desfechos clínicos avaliados:** óbito, tempo de internação (dias), tempo de internação em uso de SN (dias), data do início e fim do suporte nutricional, intervalo entre a admissão hospitalar e o início do suporte nutricional (dias), pacientes que iniciaram SN em menos ou até 48 horas e pacientes que iniciaram após 48h da admissão, encaminhamento para o CTI, complicações relacionadas ao suporte nutricional (complicações metabólicas, complicações gastrointestinais, complicações mecânicas, complicações respiratórias, complicações infecciosas e risco de síndrome de realimentação), complicações gerais (ascite e lesão por pressão), além das intercorrências (interrupção de dieta e motivos para interrupção, categorizados em motivos previstos e não previstos).
- **Dados bioquímicos**: creatinina sérica.

4.3.1. Avaliação Nutricional

Os dados antropométricos incluíram peso (Kg), altura (cm), circunferência do braço (CB) (cm), circunferência da panturrilha (CP), índice de massa corporal (IMC) (Kg/m²) e diagnóstico nutricional determinado pelo nutricionista do setor, conforme avaliação nutricional. Peso e altura foram utilizados se informados, medidos ou estimados, segundo o prontuário (94).

O IMC foi calculado e agrupado em cinco categorias de acordo com sua classificação (95) para adultos e idosos (96). As categorias foram: baixo peso, peso adequado/eutrofia, sobrepeso e obesidade. Já o diagnóstico nutricional apresentou grande variabilidade, por isso também foi agrupado para facilitar o entendimento. As categorias foram: suspeita de desnutrição; desnutrição moderada (incluindo

desnutrição leve e desnutrição); desnutrição grave; eutrofia e sobrepeso (assumindo sobrepeso e obesidade como uma categoria). Esses dados são representativos da primeira e última avaliação nutricional desses pacientes quando iniciaram o suporte nutricional.

4.3.2. Equações de Estimativa de Massa Muscular

Uma revisão sistemática da literatura recém-publicada (97) objetivou identificar equações de estimativa de massa muscular a partir de dados antropométricos. ara a utilização no presente estudo, as equações identificadas na revisão sistemática foram avaliadas e como critério de seleção, aquelas com coeficiente de determinação (r^2) maior ou igual a 0,78 e o menor erro padrão da estimativa (SEE) possível, foram selecionadas. Além do critério de seleção descrito acima, as equações foram selecionadas com base nos dados antropométricos e exames bioquímicos disponíveis nos prontuários dos pacientes acompanhados pela Comissão de Suporte Nutricional do Hospital das Clínicas da UFMG.

Ao todo 11 fórmulas, propostas por quatro autores, foram incluídas neste trabalho (Quadro 1). Cada uma das equações de estimativa de massa muscular selecionadas, estima uma fração de massa muscular diferente, sendo: tecidos moles magros, massa livre de gordura, massa magra apendicular e massa muscular esquelética. Todas as fórmulas são destinadas a homens e mulheres e utilizam dados de peso (Kg), altura (m ou cm) e/ou IMC (kg/m^2). Porém, apenas a equação referente a massa muscular esquelética possui variações segundo a etnia. Todas as equações selecionadas foram validadas previamente em populações específicas. No momento em que os dados antropométricos dos pacientes foram aplicados às equações, foram necessários ajustes nos dados de uma delas, no que diz respeito às unidades de medida da variável altura, devido à discrepância dos valores de MM obtidos. Sendo assim, na fórmula de Li (98) os dados da altura foram transformados de centímetros para metros.

Quadro 01 - Equações de estimativa da massa muscular.

Desenvolvimento e validação (Autor e ano)	Dados das equações	Equações
Tecidos Moles Magros		
Janmahasatian et al., 2005	P, IMC	(H) = (9270 × P (kg)) ÷ [6680 + (216 × IMC)]
		(M) = (9270 × P (kg)) ÷ [8780 + (244 × IMC)]
Massa Livre de Gordura		
Li et al., 2019	I, A, P	−5.382 − 0.037 x I (anos) + 0.154 x A (m)) + 0.502 x P;
Massa Magra Apendicular		
Kulkarni et al., 2013	P, A, I	(H) (Kg) = −13.432 – (0.0445 × I (anos)) + (0.200 ×P) + (0.140 × A (cm))
	P, A, I	(M) (Kg) = −9.852 – (0.028 × I (anos)) + (0.170 × P) + (0.102 × A (cm))
Massa Muscular Esquelética		
Lee et al., 2000	P, A, I, G	(H) (kg)= 0,244 x P (kg) + 7,80 x A (m) - 0,098 x I (anos) + 6,6 x G (1 para H) + Etnia (-1,2 para asiáticos, 1,4 para Negros e americanos e 0 para brancos e hispânicos) - 3,3.
		(M) (kg)= 0,244 x P (kg) + 7,80 x A (m) - 0,098 x I (anos) + 6,6 x G (0 para M) + Etnia (-1,2 para asiáticos, 1,4 para Negros e americanos e 0 para brancos e hispânicos) - 3,3.

A: altura; H: homem; I (anos): idade; IMC: índice de massa corporal; G: gênero;M: mulher; P: peso;

Assim, os dados coletados foram aplicados às equações para estimar a massa muscular dos pacientes em suporte nutricional no momento inicial e final da internação. As equações estimaram a massa muscular em kg, e esta foi transformada em percentual do peso corporal dividindo o valor encontrado pelo peso do paciente e multiplicando por 100.

4.3.3. Infusão Nutricional

Os dados referentes ao suporte nutricional foram coletados diariamente das evoluções nutricionais de cada paciente durante todo o período que permaneceram em uso de suporte nutricional. A média da prescrição dos pacientes foi estimada por meio da seguinte fórmula:

Soma do valor bruto das calorias e proteínas / Nº de dias em que houve prescrição

A infusão calórica e proteica foi estimada da mesma forma. O balanço calórico e proteico foi calculado como:

Média da infusão de calorias e proteínas do período em SN - Média do valor das prescrições do período em SN

A proporção do balanço calórico e proteico foi estimada pela:

*Valor encontrado na fórmula do balanço calórico e proteico / Valor das prescrições do período em SN * 100*

Pacientes sem informação sobre mediana de consumo foram excluídos da análise do balanço calórico e proteico.

Quando a infusão de NE e/ou NP foi avaliada em proteínas e calorias por quilo (Kcal/kg e g/kg) e adequação da ingestão (%), a infusão foi calculada como:

Soma dos valores energéticos e proteicos disponíveis nos prontuários / Nº de dias com esses dados / Média do peso corporal durante a internação hospitalar.

A adequação foi calculada como a razão percentual entre a mediana do que foi infundido e do que foi prescrito.

Os dias sem infusão de dieta, ou seja, jejum, foram incluídos e contabilizados como 0% de adequação. Pacientes sem informações sobre consumo foram excluídos das análises.

4.3.4. Desfechos Clínicos

Para os desfechos clínicos foram coletados os dados de mortalidade e internação na UTI na forma de taxa (%); já o tempo de internação hospitalar, tempo de internação em uso de SN e intervalo entre a internação e o início do uso do suporte nutricional, em dias. A última variável foi categorizada entre os pacientes que iniciaram o suporte nutricional em até ou menos de 48 horas da internação e entre aqueles que iniciaram em mais de 48 horas. Além disso, foram coletados o número de interrupções

da dieta e motivos, e categorizadas em interrupções esperadas e inesperadas e o número de complicações por dia de internação com suporte nutricional. As interrupções foram analisadas sob a forma de taxas de ocorrência, calculadas como o número total de interrupções dividido pelos dias de permanência hospitalar em suporte nutricional. Os motivos esperados para a interrupção da dieta incluíam pausas para procedimentos e exames, para monitoramento da ingestão oral, por falta de prescrição ou pausas para confirmação do posicionamento do cateter. Os motivos inesperados para interrupção da dieta incluíram interrupções por instabilidade hemodinâmica, distensão abdominal, estase, diarreia ou vômito, além de exteriorização ou obstrução do cateter. O risco de síndrome de realimentação e presença de lesão por pressão foram analisados como variáveis categóricas, calculadas como o número de pacientes com ou sem essas condições.As complicações relacionadas ao suporte nutricional foram: complicações metabólicas (incluindo hiper e hipoglicemia, hiper e hipocalemia, hiper e hipofosfatemia, hiper e hiponatremia e hipertrigliceridemia - esses dados foram considerados quando descritos nos prontuários); complicações gastrointestinais (como prisão de ventre - mais de 3 dias sem evacuação, diarreia - 3 ou mais episódios de fezes líquidas no dia, distensão abdominal, volume residual gástrico, esteatose, colelitíase, gastroparesia, náuseas e vômitos); complicações mecânicas (exteriorização e obstrução do tubo); complicações respiratórias (aspiração, pneumotórax e broncoaspiração) e complicações infecciosas (febre - temperatura corporal acima de 38 graus). As complicações foram analisadas em frequência absoluta e na forma de taxas de ocorrência, calculadas como o número total da complicação dividido pelos dias de internação em uso de SN.

Ressalta-se que os dados de transferência para UTI referem-se aos casos em que, durante a internação em uso de SN, o paciente permaneceu em leito de UTI. Nesta situação, foram excluídos da análise desta variável aqueles já internados na UTI.

4.4. Análises Estatísticas

Todos os dados foram analisados no software estatístico Statistical Package for Social Sciences (SPSS®) versão 20.0 (Chicago, IL, EUA). O nível de significância adotado para rejeição da hipótese nula foi $p \leq 0,05$ e intervalo de confiança de 95%.

As variáveis contínuas foram testadas quanto à normalidade por meio do teste de Shapiro-Wilk, e a distribuição foi assimétrica para todas as variáveis, exceto a CP. As variáveis quantitativas foram descritas como mediana (intervalo interquartil (IIQ) – P25 a P75) ou média e desvio padrão (DP). As variáveis categóricas foram descritas em frequência absoluta e relativa.

A análise de correlação foi realizada por meio do teste de Spearman para verificar a correlação do consumo calórico e proteico(/Kg) e adequação (%); a correlação entre as variáveis de exposição e os desfechos clínicos de acordo com o intervalo entre a admissão e o início do suporte nutricional, com correlações de sensibilidade de acordo com pacientes que receberam suporte nutricional em 48 horas ou mais. Também foi realizada análise de correlação com alterações de massa muscular (∆%) e alterações de CB, CP e creatinina. Além disso, correlações da ingestão calórica e proteica e suas adequações, que foram correlacionados com alterações na massa muscular (∆%).

As correlações foram consideradas diretas quando apresentavam coeficiente de correlação positivo, e indiretas quando o coeficiente era negativo. As correlações foram fracas quando o coeficiente de correlação foi <0,300, moderadas, se coeficiente entre 0,300 e 0,500, e fortes se >0,500 (99). Para as análises foram utilizados dados de consumo de kcal e gramas por kg e adequação calórica e proteica em % de pacientes agrupados por classificação de tercis.

O teste de Mann-Whitney para amostras independentes, foi realizado para comparar as medianas dos aspectos dietéticos e clínicos de acordo com a perda ou manutenção/ganho de massa muscular durante a internação. Também foi aplicado para comparar os dados dos desfechos clínicos segundo o intervalo entre a admissão e o início do suporte nutricional (pacientes que receberam suporte nutricional em 48 horas ou mais). E por fim, realizado para comparar as interrupções durante a internação e o intervalo entre a admissão e o início do suporte nutricional, considerando o grupo de pacientes que faleceram e os que sobreviveram, os internados na UTI e os não internados durante a internação, bem como aqueles que apresentaram ou não risco de síndrome de realimentação e lesão por pressão.

Ainda para amostras independentes, foi utilizado o teste de Kruskal-Wallis para comparar aspectos dietéticos e clínicos durante a internação, considerando faixas de adequação calórica e proteica. E para o consumo por quilograma de peso foi realizada

a mesma análise. O teste de Wilcoxon foi utilizado para comparar o percentual de massa muscular no início e no final da internação em suporte nutricional. De acordo com a alteração da massa muscular durante a internação, aqueles que tiveram variação percentual negativa na massa muscular (∆%) foram classificados como grupo que perdeu massa muscular e aqueles sem variação ou com alteração positiva, como grupo que ganhou ou manteve a massa muscular. O teste qui-quadrado foi aplicado às variáveis categóricas como óbito, internação em UTI, cuidados paliativos, risco de síndrome de realimentação e lesão por pressão conforme o momento de início do suporte nutricional.

O consumo e a adequação de calorias e proteínas também foram apresentados como tercis. A divisão dos tercis foi realizada através do registro das variáveis no software estatístico, portanto, a seleção dos grupos e valores foi realizada de forma automática, onde foi determinado o número de grupos (3 tercis). Os pacientes foram agrupados conforme o consumo de kcal e gramas por kg, e adequação calórica e proteica em %, em três grupos com base na classificação por tercis. O primeiro tercil foi considerado baixo consumo/adequação, o segundo tercil como moderado e o terceiro tercil como alto consumo/adequação.

Por fim, foram realizados modelos de regressão considerando os três grupos de adequação calórica e proteica e a ingestão por Kg; Intervalo entre a admissão e o início do suporte nutricional, as interrupções esperadas e as interrupções inesperadas como variáveis independentes. Para modelos de regressão linear, as taxas de complicações, tempo de internação, tempo de internação no SN e alterações da massa muscular foram utilizadas como variáveis dependentes.

O nível de significância adotado para entrada no modelo foi $p<0,2$, sendo utilizado o método forward. Nos modelos de regressão logística binária, as variáveis dependentes foram categorias de alteração da massa muscular, óbito, risco de síndrome de realimentação e lesão por pressão, cuidados paliativos ou transferência para terapia intensiva. Para esta última variável, os modelos de regressão foram construídos excluindo uma variável setor, portanto apenas a idade e o sexo foram incluídos como ajustes.

1. RESULTADOS E DISCUSSÃO

Visando responder os objetivos desta dissertação, nesta seção são apresentados três artigos originais escritos conforme as normas das respectivas revistas de interesse para a submissão. O Artigo Original 1, intitulado **“Association between nutritional intake and muscle mass in patients using nutritional support: A prospective cohort study”**, foi submetido à revista “*Journal of Parenteral and Enteral Nutrition*” e está em processo de revisão. O Artigo Original 2, cujo título é **“Association of adequacy and intake of calories and protein with clinical outcomes of patients using nutritional support: prospective study”**, que foi submetido à revista “*Clinical Nutrition*”. Finalmente, o Artigo Original 3, **“Challenges of nutritional support administration and clinical outcomes during hospitalization: a prospective study”**, que será submetido á revista “Clinical Nutrition”.

5.1. Artigo Original 1

Title:

"Association between nutritional intake and muscle mass in patients using nutritional support: A prospective cohort study"

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Conflict of Interest

All authors declare no conflict of interest.

ABSTRACT

Objective: The present study aimed to evaluate the association between muscle mass variation, estimated by different equations, during hospitalization with the caloric and protein intake and clinical and nutritional outcomes of patients using nutritional support.

Methods: A prospective observational study with patients over 18 years in use of enteral and/or parenteral nutritional therapy and monitored by the Nutritional Therapy Committee between 14 December 2021 and 14 December 2022. Data were collected from the electronic records and were applied in 11 equations to estimate the four different portions of muscle mass of patients receiving nutritional support at the beginning and the end of hospitalization.

Results: A total of 261 were evaluated with a median of 61.0 (49.0 - 69.75) years old, 106 were women (40.6%). According to the nutritional diagnosis, several participants had severe malnutrition (39.5%). The most muscle mass estimation equations indicated a reduction of muscle mass during hospitalization. All patients presented negative caloric and protein balances during hospitalization. But greater protein intake increased the lean soft tissue. Also, the greater the number of infections, metabolic complications, and scheduled diet interruption, the greater was the chance of losing muscle mass.

Conclusion: There can be an association between the variation in muscle mass and caloric and protein intake during hospitalization of patients using nutritional support. In addition, variation in muscle mass was associated with complications from nutritional support. The results emphasize the importance of anthropometric measurements to estimate muscle mass when other methods are not available.

Keywords: Muscle mass. Nutritional Support. Hospital Nutrition. Malnutrition. Anthropometry.

1. Introduction

Malnutrition is an alarming and highly preventable problem in hospitalized patients. In emerging and developed countries, it is estimated that this condition varies from 28% to 50%, depending on the characteristics of the population and the method used for nutritional diagnosis.[1,2] In Brazil, the Brazilian Nutritional Assessment Survey (IBRANUTRI), a pioneering cross-sectional, multicenter study involving 4,000 hospitalized patients in 12 Brazilian states and the Federal District, revealed that 48.1% of patients hospitalized in the public network had some degree of malnutrition.[3] Nevertheless, malnutrition is a worldwide problem. A multicenter prospective observational cohort study included 800 patients admitted to four Colombian hospitals and found a prevalence of 24.62% of malnutrition at hospital admission (.[2] In the study by Kang (2018)[4] with 300 hospitalized patients in Korea, the prevalence of malnutrition was 22.0%.

Elderly, oncologic, and critically ill patients are most affected by malnutrition. This is due to their greater vulnerability to the effects of hospitalization, the metabolic effects of the disease, and reduced nutritional intake.[5,2] In catabolic states, changes in protein synthesis and muscle degradation occur, resulting in loss of strength and muscle mass .[5] Low muscle mass is associated with a worse prognosis, a decline in the quality of life, higher mortality and morbidity rates, more hospital costs, and increased length of stay.[1] Skeletal muscle strongly influences metabolic and physical health. Therefore, it is considered a good predictor of general health status.[6]

Faced with the adverse effects of malnutrition and low muscle mass in hospitalized patients, it is necessary to use reliable tools to assess muscle properties in clinical practice. Currently, there are several ways to quantify muscle mass and body composition, such as electrical bioimpedance, computed tomography, magnetic resonance imaging, and dual-energy X-ray absorptiometry.[10] However, these methods are expensive and require a trained operator to handle the test instruments. Also, they may be influenced by external factors such as age, weight, fasting state, hydration, and environmental temperature.[6] Although there is no gold standard method for measuring muscle mass, predictive equations using anthropometric measurements have emerged with numerous advantages, including their low cost and feasibility. Also, they are a valid method for the hospital environment and are non-invasive.[1] Even though it is known that early diagnosis and approach are essential for preventing and managing malnutrition in hospitalized patients,[11] there is still no consensus in the literature on the treatment for low muscle mass. Studies have shown that the combination of a good caloric and protein intake and physical training can be effective.[12] The ESPEN guidelines suggest that malnourished patients should receive individualized nutritional counseling, and nutritional

support should be considered when it is not possible to reach the protein and energy needs according to the clinical status, prognosis, and preferences of individuals and their families.[13] However, the association of caloric and protein intake with muscle mass changes during hospitalization and how this change could influence clinical outcomes is not clear in the literature.

Thus, the hypothesis of this study is that the low consumption of calories and proteins results in a reduction of muscle mass and, consequently, this reduction negatively impacts the clinical outcomes of patients. Therefore, the present study aimed to evaluate the association between muscle mass variation, estimated by different equations, during hospitalization with the caloric and protein intake and clinical and nutritional outcomes of patients using nutritional support.

2. Materials and methods

2.1 Study Design

This is a prospective observational study carried out in a single hospital (Hospital das Clínicas of the Federal University of Minas Gerais – HC-UFMG). The study was approved by the Ethics Committee of the Federal University of Minas Gerais (CAAE 7966620.4.0000.5149). The HC-UFMG is a public and general university hospital that performs clinical care, teaching and research activities. It is a reference in the treatment of medium and high complexity pathologies. It has 504 beds for elective (clinical and surgical) and emergency hospitalizations, with90 intensive care beds (adult and pediatric). In 2019, it performed an average of 1500 hospitalizations, 750 surgeries and 36000 consultations.

The eligible participants were informed about the research competencies. Accessible language was used, and doubts were resolved, following the ethics and confidentiality of data as recommended by the Guidelines and Regulatory Norms for Research Involving Human Beings of the National Health Council.[14] All participants and/or guardians who agreed to participate in the project signed the Informed Consent form, and data was collected only after this stage.

2.2 Sample

The participants eligible for the study were patients of both genders admitted by the Nutritional Support Commission. They were 18 years old or older and were using enteral and/or parenteral nutritional therapy for at least 24 hours, associated or not with oral therapy. Also, as inclusion criteria, it was essential to sign the Informed Consent Form and have at least one nutritional evaluation during the period using nutritional support.

Exclusion criteria were the following: patients who received only oral nutritional therapy, pediatric patients, pregnant women, patients/responsible family members who refused to sign the Informed Consent Form, and patients without measurements or an estimation of their weight. Patients who were re-hospitalized after having already joined the project were not included again. A patient flowchart was developed to illustrate the inclusion process in the study and it can be seen in the supplementary material (Figure 1).

2.3 Data collection

All collected data were secondary information obtained from the electronic medical records of patients hospitalized at the Hospital das Clínicas of the Universidade Federal de Minas Gerais (UFMG). Patients included were hospitalized between 14 December 2021 and 14 December 2022.

Data collection was carried out daily, except on weekends, by a team of trained researchers, including students, professors, and professionals from the hospital.

The identification of eligible patients was carried out by consulting the map of patients using enteral and parenteral diets generated daily by the Nutritional Therapy Commission of the hospital. After identifying and signing the Informed Consent Form, the researchers collected data from clinical and electronic records. No data regarding diet was requested directly from the patient, their companion, or the professionals who followed them. The collected information was sent in an electronic form on Google docs®, and after filling it out, it was computed in a database in the Microsoft® Excel program.

2.3.1 Clinical data

The following data were collected from the electronic records: (1) demographic data (gender, age, race/color, date of birth, location); (2) hospitalization data (registration number, date of hospitalization, bed, hospitalization sector, clinical comorbidities, past medical history, presence of neoplasia); and (3) biochemistry data (serum creatine (SCre)).

Clinical outcomes were as follows: death, length of stay, length of stay in nutritional support, complications related to nutritional support such as metabolic complications (including hyper- and hypo-glycemia, hyper- and hypo-kalemia, hyper- and hypo-phosphatemia, hyper- and hypo-natremia, and hyper-triglyceridemia), gastrointestinal complications (constipation, diarrhea, bloating, gastric residual volume, steatosis, cholelithiasis, gastroparesis, nausea, and vomiting), mechanical complications (tube exteriorization and obstruction), respiratory complications (aspiration, pneumothorax, and broncho-aspiration), infectious complications (fever and catheter infection), risk of refeeding syndrome, and general complications (ascites

and pressure injury), in addition to intercurrences (diet interruption and reasons for an interruption, categorized into foreseen and unforeseen reasons).

2.3.2 Nutritional data

Data on nutritional status and nutritional prescriptions were also collected from the electronic records.

The nutritional status data were compiled at two times: at the beginning of nutritional support, immediately after hospitalization, and upon nutritional support discharge. All of the nutritional evaluations were carried out by the hospitals' nutritionists. Data collected from the records included weight (Kg), height (cm), mid-arm circumference (MAC) (cm), calf circumference (CC) (cm), BMI (Kg/m²), and a nutritional diagnostic determined by the hospital nutritionist, according to the nutritional assessment protocol. Weight and height were used if they were informed, measured, or estimated. If a patient had only a register of the ideal body weight on his/her hospital record, it was excluded from the sample.

The exposure of interest in this study was the caloric and protein intake of patients receiving nutritional support. Data regarding nutritional support were collected daily during the whole time of nutritional support use. The type of support (enteral or parenteral, associated with the oral route or not), the prescription, and the consumption of calories and proteins were collected daily. The median prescription and intake of the patients were estimated using the number of days with the prescription and the number of days assessing caloric and protein intake by 24 h records. The caloric and protein balance was calculated as the difference between the median intake and the median value prescribed. The proportion of caloric and protein balance was estimated by dividing the previously described difference by the prescribed number and multiplying by 100. Patients with no information about median consumption were excluded from the analysis of the caloric and protein balance.

2.4 Muscle mass estimation equations

The primary outcome was the change in muscle mass, defined by the two-point analysis using predictive equations. Secondary outcomes consisted of clinical outcomes and complications previously mentioned in the clinical data. The muscle mass estimation equations were selected from a recent systematic review (PROSPERO CRD42021257200) that aimed to identify equations for estimating muscle mass from anthropometric data. As a criterion for selecting the equations for the present study, the equations must have had a coefficient of determination (r^2) greater than or equal to 0.75 and the lowest standard error of the estimate (SEE) among the equations with that r^2. In addition, the selection must estimate muscle mass from

anthropometric data and biochemical tests available in the medical records of patients monitored by the Nutritional Support Committee of the Hospital das Clínicas of UFMG.

A total of 11 (including the gender and ethnicity variations) formulas proposed by four authors [9,15,16,17]were included in this work (**Table S1**). Each of the selected muscle mass estimation equations assesses a different muscle mass portion–namely, LST, FFM, ALM, and SMM. All formulas are intended for men and women and use weight (Kg), height (m or cm), and/or BMI (kg/m²) data. However, only the equation referring to SMM has variations according to ethnicity. All selected equations were previously validated in specific populations, as described in Table S1. When applying the equations to anthropometric data, adjustments were necessary for one of them, regarding the height measurement units, due to the discrepancy of muscle mass values obtained. Therefore, in Li's (2019)[17] formula, height data were transformed from centimeters to meters. The adjusted equations can be seen in **Table S1**.

Thus, the collected data were applied in equations to estimate the four different portions of muscle mass of patients receiving nutritional support at the beginning and the end of hospitalization in order to allow a comparison of these moments. The equation estimated the muscle mass in Kg, and it was transformed into a percentage of body weight.

2.5 Statistical analysis

All data were analyzed utilizing SPSS version 20.0 (Chicago, IL, USA). The significance level adopted for rejecting the null hypothesis was $p \leq 0.05$ and confidence interval of 95%.

Continuous variables were tested for normality using the Shapiro-Wilk test and most of which had an asymmetrical distribution. Quantitative variables were described as median (interquartile range – P25 to P75) or mean and standard deviation (SD). Categorical variables were described in absolute and relative frequency. Correlation analysis with muscle mass changes (∆%) and MAC, CC and SCre changes were performed using the Spearman test. Also, the caloric and protein intake and their balance were correlated with muscle mass changes (∆%). The Wilcoxon test was used to compare the percentage of muscle mass at the beginning and end of hospitalization in nutritional support. According to the change in muscle mass during hospitalization, those who had a negative percentage change in the muscle mass (∆%) were classified as the Lost group and those with no variation or with positive change, as maintained/gained muscle mass group. For independent samples, the Mann-Whitney test was used to compare the dietary and clinical aspects according to loss or maintenance/gain of muscle during hospitalization. The same comparison was made using chi-square for categorical variables.

Finally, univariate linear regression was performed considering the muscle mass changes or length of hospital staying as dependent variables. The adopted significance level

to enter the model was p<0.200, and the forward method was used. Binary logistic regression models were performed with muscle mass changes categories and death as dependent variables. The Kaplan-Meier model was used to estimate the survival rate in relation to the muscle mass variation groups (muscle mass loss and maintenance/gain group) during hospitalization.

3. Results

A total of 290 patients were eligible. However, only 261 presented data to apply in the muscle mass equations, and they were evaluated (**Figure S1**). Of the 261 patients, 106 were women (40.6%) and 155 were men (59.4%). The age of participants ranged from 18 to 90 years, with a median of 61.0 (49.0 - 69.75) years old. Sixty-seven patients were hospitalized in the intensive care unit (25.7%), and 109 patients had some type of neoplasm (41.8%). BMI ranged from 12.1 to 44.4 kg/m² with a median of 22.5 (19.0 - 26.2) kg/m², and most of them were classified as normal weight. (39.8%), followed by underweight (36.4%). According to the nutritional diagnosis given by the institution's protocol, several participants had severe malnutrition (39.5%), followed by normal weight (22.5%), moderate malnutrition (20.2%), presumed malnutrition (9.7%), and overweight (8.1%). The median length of a hospital stay with nutritional support was 23 days, and the total median length of a hospital stay was 32 days. The rate of death was 31.8%. More details and other data can be seen in **Table 1.**

Table 1. General characteristics of the sample.

Age (years)	61 (50.5 - 71) *
Gender	
Female (%)	106 (40.6)
Male (%)	155 (59.4)
Ethnicity	
White	244 (93.5)
other	17 (6.5)
Hospitalization sector	
Intensive care unit (%)	67 (25.7)
Clinical admission (%)	194 (74.3)
Cancer patients (%)	109 (41.8)
Nutritional Diagnosis	

Suspected Malnutrition	25 (9.7)
Moderate Malnutrition	52 (20.2)
Severe malnutrition	102 (39.5)
Normal weight	58 (22.5)
Overweight	21 (8.1)
Type of nutritional therapy	
Enteral nutrition (%)	195 (74.7)
Enteral and oral nutrition (%)	34 (13.1)
Parenteral nutrition (%)	23 (8.8)
Parenteral and oral nutrition (%)	9 (3.4)
Total Hospitalization Time (days)	32 (20 - 47.75) *
Length of Stay at the Nutritional Support (days)	23 (12 - 37) *
Death Rate (%)	83 (31.8)
Complications	9 (4.0 – 20.5)
Nutritional support complications	8.0 (3.5 – 17.5)

Data presented as number and proportion. *Data presented as median and interquartile range.

3.1 Muscle mass estimation

Table 2 presents the muscle mass estimates (%) for each equation at the baseline and final moment of nutritional support. The number of patients who had data for the initial assessment (261) was higher than those who had data for the final assessment (158). The median LST in the baseline (72.58%) was lower than at the hospital nutritional support discharge (73.25%; $p = 0.016$). On the other hand, FFM and ALM were significantly higher in the baseline than at the hospital discharge ($p = 0.014$ and $p = 0.006$, respectively). The median SMM of the sample was not statistically different during the hospital stay.

Spearman correlations were performed between MM estimates and the anthropometric and biochemical data at the baseline and at the nutritional support discharge. The MM changes were correlated with the changes observed in MAC, CC, and SCre during hospitalization. In assessing percentage change (Δ%), MAC correlated with all three MM fractions. There was an inverse and moderate correlation between MAC and LST ($n = 131$; $r = -0.369$; $p<0.001$), and a direct and moderate correlation of MAC with FFM ($n = 131$; $r = 0.363$; $p<0.001$) and ALM ($n = 131$; $r= 0.377$; $p<0.001$). Regarding CC, there were only significant correlations between percentage variation with FFM ($n = 139$; $r= 0.177$; $p = 0.044$) and ALM ($n = 131$; $r = 0.187$; $p =$

0.034). Both were weak and direct correlations. There was no significant correlation between the MM estimations and SCre (n = 102). Sensitivity analysis (**Table S3**) was performed, including only patients without upper limb edema in the MAC analyses, only those without lower limb edema in the CC analysis, and only those without kidney disease in the SCre analysis. There was an intense and inverse correlation of the percentage variation between MAC and LST (r= -0.466; p=0.009) for patients without upper limb edema. As for FFM and ALM, the correlations were direct and moderate (r= 0.463; p=0.010 for both). In the CC, no significant correlations were observed. Also, there was no significant correlation between any of the MM fractions and SCre.

Considering the percentage of change of muscle mass during hospitalization, 122 patients maintained or gained LST and 36 lost it. As for FFM, 105 patients maintained or gained and 53 lost it. Finally, 102 patients maintained or gained ALM and 56 lost it.

Table 2. Comparison of the percentage of muscle mass by estimating equations and its variation in change in the initial and final moments of hospitalization of patients on nutritional support.

	Muscle mass					Change
	(N)	**Baseline**	**(N)**	**Final**	**p-value**	**Δ %**
Lean soft tissue mass (%)	261	72.58 (63.77 - 79.05)	158	73.25 (63.29 - 81.18)	0.016	0.002 (-0.182 - 0.201)
Fat-free mass (%)	261	38.27 (35.94 - 40.13)	158	37.78 (35.48 - 39.88)	0.014	0.00 (-0.151 - 0.071)
Appendicular lean mass (%)	261	35.73 (31.76 - 39.72)	158	35.65 (31.30 - 40.22)	0.006	0.00 (-2.600 - 0.116)
Total skeletal muscle mass (%)	261	38.44 (30.18 - 43.15)	158	38.36 (30.12 - 42.59)	0.481	0.00 (-0.734 - 1.170)

Data presented as median and interquartile range. Wilcoxon test.

3.2 Muscle mass estimation and caloric and protein intake

The first outcome was analyzed as group, considering the percentage of change of muscle mass during hospitalization, as described above. The consumption of calories and protein of the two groups (lost *versus* gain/maintained muscle mass) were compared. **Table 3** presents the average calorie and protein intake, and the balance of it, of the patients according to their muscle mass change categorization. No statistical difference was observed between the groups. However, a greater median intake of calories and protein was observed in those who

gained or maintained LST, and the opposite was seen regarding FFM and ALM. Concerning the caloric and protein balance, it was observed that the median in all groups indicated a negative balance. Looking only at the percentage balance, except for LST, the group who maintained or gained muscle mass had a smaller imbalance in all other muscle mass.

Table 3. Median intake and calorie and protein balance according to change of muscle mass.

	Lean Soft Tissue			Fat-free mass			Appendicular lean mass		
Variables (n)	**Lost (36)**	**Maintained or gained (122)**	**p value**	**Lost (53)**	**Maintained or gained (105)**	**p value**	**Lost (56)**	**Maintained or gained (102)**	**p value**
Median Intake									
Calories (kcal/day)	1161.15 (931.25 1482.45)	1268 (908.90 - 1454.35)	0.394	1311.50 (935.50 -1512.30	1242.18 (874.35 - 1436.70)	0.174	1329.20 (980.2 - 1514.9)	1225.21 (967.5 - 1427.1)	0.068
Calories (% of prescription)	76.43 (52.52 - 92.03)	79.55 (62.36 - 88.99)	0.736	79.30 (63.30 - 88.56)	77.48 (60.00 - 91.30)	0.936	78.34 (63.32 - 88.60)	77.74 (58.87 - 91.22)	0.916
Protein (g/day)	55.70 (36.45 -75.73)	64.85 (45.70 - 76.60)	0.278	67.50 (46.15 - 79.47)	61.55 (44.01 - 75.19)	0.234	67.18 (47.09 - 80.75)	61.40 (42.5 - 75.0)	0.164
Protein (%)	71.29 ± 31.43	71.41 ± 23.53	0.980	72.01 ± 21.18	71.06 ± 27.50	0.827	72.39 ± 21.17	70.82 ± 27.66	0.714
Median balance intake									
Caloric balance (kcal/day)	-353.1 (-588.7; -133.6)	-319.8 (-564.9; -175.4)	0.783	-330.9 (-583.0; -223.3)	-387.6 (-573.6; -133.1)	0.372	-334.9 (-591.5; -223.0)	-319.4 (-571.1; -133.6)	0.315
Caloric balance (% of prescription)	-21.9 (-38.6; -8.4)	-24.5 (-364; -10.9)	0.968	-22.3 (-36.0; -12.6)	-21.0 (-37.2; -8.4)	0.506	-22.4 (-37.1; -12.2)	-20.9 (-36.8; -8.4)	0.511
Protein balance (g/day)	-18.3 (-30.0; -5.9)	-18.0 (-35.0; -7.2)	0.581	-20.8 (-34.0; -11.2)	-17.3 (-34.8; -5.4)	0.182	-20.8 (-35.0; -11.1)	-16.8 (-34.8; -5.6)	0.173

Protein balance (%)	-22.0 (-40.0; -9.4)	-24.1 (-40.4; -8.4)	0.814	-26.2 (-37.1; -12.6)	-20.9 (-41.8; -6.7)	0.310	-26.6 (-37.3; -11.7)	-20.6 (-41.1; -6.7)	0.315

Data presented as median and interquartile range or mean ± standard deviation. Mann Whitney U Test.

Spearman's correlations were performed between the consumption of calories and protein and the changes in muscle mass in the two moments (**table S4**). No correlation was seen between the muscle mass changes and the median intake of calories and protein. There was also no correlation between the average energy and protein balance and muscle mass variations.

Multivariate linear regression analysis was performed to comprehend the determinants of muscle mass changes (Δ%). Independent variables that previously had some association with the muscle mass or with clinical relevance to muscle mass were added to the model. When LST (Δ%) was used as the dependent variable, the total protein intake during the day was significantly associated with the increase of this parameter regardless of gender, age, and length of hospital stay **(Table 4**).

Table 4. Protein Intake and its association with the variation in muscle mass.

Variable	Null Model			Adjusted Model[1]			Adjusted Model[2]			Adjusted Model[3]		
	R^2	β	P-value	R^2	β	P-value	R^2	β	P-value	R^2	β	P-value
Lean Soft Tissue (Δ%)												
Protein intake (g/day)	0.029	0.170	0.036	0.018	0.173	0.034	0.013	0.171	0.036	0.008	0.164	0.048

Simple linear regression model. Null Model: each variable was inserted in the linear regression analysis without the addition of any adjustment variable.
Adjusted Model[1]: adjusted for age;
Adjusted Model[2]: adjusted for age and sex;
Adjusted Model[3]: adjusted for age, sex and total length of hospital stay. R^2= R-squared

3.3 Muscle mass and clinical outcomes

The clinical outcomes, secondary outcomes, of patients who lost muscle mass were compared to the clinical outcomes of those who gained or maintained, as can be seen in **Table 5.** Patients who lost LST presented fewer metabolic complications (p=0.002) and a different number of infectious complications (p=0.013) than those who gained or maintained. The median number of infectious complications was equal to zero in both groups. Therefore, when looking at the total number of infectious complications among those who lost LST, the number was lower than for those who gained or maintained [1(2.8%) vs. 24(19.7%), respectively]. Regarding FFM, the ones who lost this muscle mass presented more total complications (p = 0.035), more complications related to nutritional support (p = 0.036), more metabolic complications (p = 0.008), and more scheduled reasons for nutritional support interruption (p = 0.017) than those who maintained or gained FFM. Finally, those who lost ALM presented more metabolic complications (p = 0.048) and more scheduled reasons for nutritional support interruption (p = 0.038) than the ones who gained or maintained the ALM.

Table 5. Clinical outcomes of hospitalization according to the variation in muscle mass of patients receiving nutritional support.

	Lean Soft Tissue			Fat-free mass			Appendicular lean mass		
Clinical outcomes (n)	**Lost (36)**	**Maintained or gained (122)**	**p value**	**Lost (53)**	**Maintained or gained (105)**	**p value**	**Lost (56)**	**Maintained or gained (102)**	**p value**
Death rate (%)[1]	30.60%	32.00%	0.999	30.20%	32.40%	0.857	28.60%	33.30%	0.594
Total length of hospital staying	31.00 (21.00 - 47.00)	35.50 (23.75 - 56.25)	0.160	36.00 (24.50 - 64.50)	34.50 (22.00 - 48.75)	0.224	35.50 (23.25 - 62.75)	35.50 (22.00 - 49.50)	0.363
Length of hospital staying with nutritional support	23.50 (12.50 - 37.75)	27.00 (16.00 - 44.25)	0.319	28.00 (18.00 - 50.50)	25.00 (15.00 - 39.50)	0.176	28.00 (16.50 - 48.50)	26.00 (15.00 - 41.25)	0.363
Total complications	8.00 (4.25 - 20.25)	13.50 (5.75 - 23.50)	0.194	14.00 (6.00 - 30.00)	10.00 (4.50 - 21.00)	**0.035**	14.00 (6.00 - 29.50)	10.00 (5.00 - 21.00)	0.120

Complications related to nutritional support	6.50 (4.00 - 17.50)	11.00 (5.00 - 22.00)	0.131	14.00 (6.00 - 25.50)	9.00 (4.00 - 18.00)	**0.036**	13.00 (5.25 - 24.25)	9.00 (4.00 - 18.25)	0.114
Metabolic complications	1.00 (0.00 - 3.00)	4.00 (0.00 - 11.00)	**0.006**	6.00 (1.50 - 14.00)	2.00 (0.00 - 7.50)	**0.008**	4.50 (1.00 - 13.50)	2.00 (0.00 - 8.00)	**0.048**
Infectious complications	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	**0.013**	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.404	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.542
Reasons for interruption									
Scheduled reasons	1.00 (0.00 - 2.00)	1.00 (0.00 - 2.00)	0.960	1.00 (0.00 - 2.50)	1.00 (0.00 - 1.00)	**0.017**	1.00 (0.00 - 2.00)	1.00 (0.00 - 1.00)	**0.038**
Unscheduled reasons	1.00 (0.00 - 2.00)	1.00 (0.00 - 2.00)	0.401	1.00 (0.00 - 2.00)	1.00 (0.00 - 2.00)	0.832	1.00 (0.00 - 2.00)	1.00 (0.00 - 2.25)	0.752

Data presented as median and interquartile range or %. Mann Whitney U Test. [1]Chi Squared Test.

Spearman's correlations were performed between the clinical outcomes and the changes in MM (**table S5**). All significant correlations were weak (< 0.3) and indicated that the higher the number of metabolic complications, total complications, and complications associated with nutritional support, the lower the muscle mass for FFM and ALM, and the greater the number of metabolic complications, the higher the LST.

Binary logistic regression analysis was performed to comprehend how clinical complications and interruption of diet (independent variables) determine the chance to lose or maintain/gain muscle mass (dependent variables). Infectious complications increased the odds ratio for patients to be in the group who lost LST (**table 6**).

Multivariate linear regression analyses were also performed to comprehend the clinical determinants of muscle mass changes (Δ%). Independent variables were clinical complications and interruption of diet or clinical characteristics related to muscle mass. Scheduled reasons for diet interruption were negatively associated with FFM and ALM changes, regardless of age, gender, energy, and protein balance. Therefore, the smaller the number of diet interruptions, the greater, or more positive, the muscle mass changes (Δ%) were during hospitalization. Also, the

multivariate linear regression analysis showed that the lower the number of complications related to nutritional support, the higher, or more positive, the muscle mass changes (Δ%) were during hospitalization, when adjusted for age.

To finalize, regression analyses were also performed to comprehend the impact of muscle mass changes (Δ%) (independent variable) on the length of hospital stays and the death rate (dependent variables). No significant association was found between these parameters and muscle mass. Survival analysis was performed between data on muscle mass variation in the groups that maintained or gained and those that lost muscle mass during hospitalization and the death time. However, none of these analyzes were significant (data not shown).

Table 6. Clinical outcomes and their association with muscle mass variation categories.

Variables	Null Models			Adjusted Models[1]			Adjusted Models[2]			Adjusted Models[3]			Adjusted Models[3]		
	R^2	β	p value	R^2	β	p value	R^2	β	p value	R^2	β	p value	R^2	β	p value
Lean Soft Tissue[a] (reference group: Lost)															
Infectious complications	0.085	2.151	0.039	0.100	2.241	0.032	0.123	2.181	0.038	0.124	2.183	0.038	0.130	2.153	0.041
Fat-free mass[b] (Δ%)															
Scheduled reasons for diet interruption	-0.187	0.035	0.020	-0.191	0.035	0.020	-0.186	0.039	0.024	-0.210	0.111	0.009	-0.209	0.111	0.009
Appendicular lean mass[b] (Δ%)															
Complications related to nutritional support	0.028	-0.169	0.037	0.029	-0.167	0.039	0.063	-0.146	0.069	0.100	-0.152	0.054	0.103	-0.147	0.063
Scheduled reasons for diet interruption	0.043	-0.206	0.010	0.043	-0.207	0.010	0.045	-0.201	0.014	0.112	-0.210	0.008	0.112	-0.209	0.009

[a]Binary logistic regression model and [b]simple linear regression model. Null Models: each variable was inserted in the linear regression analysis without the addition of any adjustment variable.
Adjusted Models[1]: adjusted for age; Adjusted Models[2]: adjusted for age and sex; Adjusted Models[3]: adjusted for age, sex and energetic balance.
Adjusted Models[4]: adjusted for age, sex, energetic balance and protein balance. R^2= R-squared. - = non-significant data.

4. Discussion

The present study explored the relationship between muscle mass, estimated by different equations, with caloric and protein intake and the association with clinical outcomes in hospitalized patients using nutritional support. The results showed that most muscle mass estimation equations indicated a reduction of muscle mass during hospitalization, but this variation was very small. In general, it was observed that all patients presented negative caloric and protein balances during hospitalization. But, although the protein intake was low for all patients, greater protein intake increased the LST. Also, the greater the number of infections, metabolic complications, and scheduled diet interruption, the greater was the chance of losing muscle mass.

In the present work, the muscle mass was estimated by three different equations. We found that although validated equations were used, the results were not very sensitive to muscle mass changes in hospitalized patients. Some equations reduced muscle mass, and others increased or had no difference. The chosen equations were validated and had a very strong accuracy in several profiles.[9,15,16,17] However, they are not specific for hospitalized patients. Using equations as a bedside method for assessing muscle mass has been reinforced rather than using an isolated method like BMI, CC, or even MAC.[18,19,20]

The SMM variation was the only one among the evaluated muscle mass portion that did not present a significant difference in the evaluated individuals. It should be noted that SMM can be measured by very sensitive imaging methods. Despite this, not all of them are effective. For example, DEXA is less sensitive to small changes in the muscle mass compared to other methods, and as it is based on ionizing radiation, it has limited viability.[21] CT presents less error in the quantification of SMM, but the amount of ionizing radiation and the cost limit its use.[6] As a method of measuring SMM, MRI quantifies SMM with good sensibility, especially in obese individuals with BMI ≥ 30 kg/m2, by quantifying large deposits of adipose tissue within the muscle mass compartment. [22] Considering that the equation [16] used to estimate SMM in this study had good accuracy in comparison to MRI and that the LST, FFM, and ALM had a statistically significant but very small change, it stands out that probably no great change in muscle mass happened with this sample of patients.

The literature points out a regular muscle mass reduction for patients in different clinical conditions, such as post-kidney transplantation,[23] patients with heart failure after an acute hospitalization,[24] COVID-19 patients,[25] and patients hospitalized with chronic obstructive pulmonary disease exacerbation.[26] In particular, malnutrition, low muscle mass, and strength are highly prevalent in hospitalized elderly patients, and it is associated with adverse outcomes.[5] It is important to consider that these studies used different methods of muscle mass assessment, such as BIA, CT, and anthropometric data. A meta-analysis [27]on muscle

mass changes in hospitalized elderly patients found evidence of a decrease in muscle mass in electively admitted patients, while no significant change in muscle mass was found in acutely admitted patients. Muscle mass was measured using BIA in all patients included in the studies of the meta-analysis. These findings show the influence of the length of stay on the muscle mass of hospitalized patients. Although the most common finding during hospitalization was a reduction of muscle mass, LST had a very small increase in our data. Similarly, the EMPOWER Study [28] evaluated 373 patients at admission and 224 at discharge, and it found an increase in ALM during hospitalization. The increase was a study bias explained by a change in hydration status measured involuntarily by the BIA, thus masking a decrease in muscle mass during hospitalization, corroborating the present study. Considering the muscle mass estimation equation used to estimate muscle mass in our study, the same bias could have happened. Therefore, the equations are not very sensitive to MM changes.

Despite these already mentioned limitations of the methods for measuring muscle mass, and especially the lack of specificity to estimate the variation in muscle mass during hospitalization, sensitivity analysis was performed in this study based on correlations for anthropometric measurements. Based on these analyses, MAC and CC results with muscle mass changes indicated that the use of more specific anthropometric measurements might be useful and feasible. Thus, these results suggest that estimation equations containing anthropometric measurements commonly used in clinical practice can contribute to the measurement of muscle mass in hospitalized patients.

The strong association between estimated muscle mass and anthropometry must be considered when using predictive equations based on these parameters. For example, the combination of MAC and hand grip strength proved to be a good anthropometric parameter to assess muscle quantity and quality. When associated, they are able to identify a decline in muscle mass and function and an increased risk of mortality, as they are less sensitive to short-term changes in body composition and reflect changes in intramuscular adipose tissue.[29] CC proved to be effective in predicting muscle mass in middle-aged and elderly adults,[30] as well as a marker of muscle mass and as a predictor of hospital readmission in clinical patients.[31]

Precisely, 41.8% of the sample consisted of patients with some form of neoplasia. The main nutritional problem of these patients is the loss of muscle mass, which directly affects the prognosis. This phenomenon is repeated in hospitalized patients, where there is a negative energy balance, and this increases the loss of muscle mass induced by weight loss. A negative imbalance of calories and protein was observed in most patients, including those who lost muscle mass and those who maintained/gained it. There is evidence that this long-term loss of muscle mass is mediated by increased muscle proteolysis rather than suppression of protein synthesis.[32] Therefore, the precise definition of nutritional needs is essential for maintaining

muscle mass and stimulating protein synthesis.[33]Nonetheless, the higher the protein intake (g/day), the greater and more positive the muscle mass change (∆%) in our sample was.

Observational data suggests that higher protein intake may be associated with reduced mortality and time to intensive care unit (ICU) discharge, in addition to stimulating protein synthesis and attenuating MM loss.[34,35,36] The FEED trial [37] prospectively randomized 60 ICU patients to receive the intervention (1.2 grams/kg protein supplementation) or standard nutritional care (no protein supplementation). The results showed that there was attenuation by 0.22 cm in loss of muscle mass (95% CI, 0.06-0.38, P = 0.01) and a reduction in the prevalence of malnutrition at ICU discharge [2 (7%) vs. 8 (28%); P = 0.04] in those who received the intervention compared with standard care, with no increase in adverse events and no harm to other outcomes.

The adverse effects of hospitalization on the muscle mass have already been reported in previous studies.[27,5,38] The high prevalence of muscle mass depletion in hospitalized patients negatively impacts prognosis, clinical outcomes, and cost.[39] Also, the contrary is true. In our study, metabolic complications, infections, and scheduled diet interruptions were directly associated with a reduction in muscle mass. The study by Xi and collaborators (2021)[40] demonstrated that muscle mass was a risk factor for general complications (odds ratio 2.44; 95% CI 1.33–4.49; p=0.004), corroborating our findings. Increased inflammation, oxidative stress, and mitochondrial dysfunction are factors that result in muscle mass atrophy.[41] Inflammation affects myocytes through the interactions of pro-inflammatory cytokines (IL-6 and TNF-α) secreted by skeletal muscle.[12] These cytokines inhibit signaling pathways and activate a catabolic cycle that affects muscle metabolism and impairs anabolic stimulation for protein synthesis.[42] Another relevant problem regarding nutritional support is the continuous interruption of diet infusion during the day. Some previous studies have described the most common reasons for stopping EN infusions.[43,44,45]

The review of Kim and collaborators (2012)[44] demonstrated that frequent interruptions in feeding occur because of surgical procedures, diagnostic tests, and feeding tube problems. The prospective observational study of critically ill patients by O'Meara (2008)[45] also reinforces that enteral nutrition was interrupted in 27.3% of the available time. The reasons were problems with small diameter feeding tubes (25.5%) and increased residual volumes (13.3%). In the study by Peev (2015),[43]carried out with ICU patients, the most common reasons for diet interruptions were (re)intubation/extubation, major interventions at the bedside, and performance of imaging tests. Only 26% of these interruptions were considered preventable, but patients who had interruptions had a greater caloric deficit and longer hospital stay compared to those who did not have dietary interruptions. Our findings identified that only the scheduled diet interruptions were associated with muscle mass loss. A prospective

observational study of 73 adult medical and surgical ICU patients receiving enteral nutrition (EN) showed that EN was discontinued during 35% of test days. The main reason was hemodynamic instability (20%).[46] The literature reinforces that metabolic complications include hemodynamic instability and are related to malnutrition.[46] Situations like hemodynamic instability are not always avoidable. However, some strategies could be done to reduce the programmed stops [47,48]aiming to guarantee a positive balance of diet infusion.[49]

Despite the careful conduction of this study, some limitations should be acknowledged. First, it should be noted that the chosen equations present peculiarities of the population in which they were developed and validated. It is important to emphasize that the population was not specific to hospitalized patients in any of them. Second, the use of anthropometric data may be a viable alternative to more robust methods; however, its use in muscle mass quantification is generally limited by its susceptibility to individual prediction errors. In addition, the predictive equations used included simple measurements - body weight, height, gender, age, and race. They did not incorporate skinfolds, serum creatinine, and handgrip strength, which, despite requiring measurement devices and specialized professionals, are described as good predictors of muscle mass.[18,31] The muscle mass measurement itself is complex, as several studies characterize it differently, making it difficult to standardize the muscle area actually evaluated. In addition, the collected data were secondary. Therefore, in cases of systematic errors in the professionals' prescription, this error was replicated, thus able to interfere with the results. Another limitation is the lack of assessment of energy expenditure of patients. This data would make it possible to carry out more robust analyzes with better accuracy of nutritional needs and, consequently, consumption would be more appropriate for the proposed need. Despite the sample being heterogeneous and not having been characterized according to the pathologies presented, sensitivity analyses were performed in order to minimize damage. For example, new correlations were made by removing patients with kidney disease and edema so they would not interfere with the analysis. Considering the large number of clinical complications, several analyzes of comparisons between groups were performed, however this may result in a high risk of type 1 error. Conclusions were made when strong associations were seen. Finally, due to the scarcity of similar studies in the literature, mainly those that evaluated muscle mass associated with nutritional prescription and consumption, it was difficult to raise hypotheses that would justify different findings.

5. Conclusion

This study revealed that hospitalized patients presented a slight loss of muscle mass during hospitalization when analyzed by muscle mass prediction equations. In addition, the caloric and protein balance was negative in most of the samples, and greater protein intake was

associated to less muscle mass depletion. Muscle mass variation was associated with complications of nutritional support. The results obtained through the prediction equations emphasize the importance of anthropometric measurements to estimate muscle mass when other methods are not available. However, prediction equations that are more sensitive to muscle mass and validated in hospitalized patients are needed to obtain greater reliability and accuracy for use in clinical practice.

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Supplemental Material

Table S1. Description of data from muscle mass prediction equations.

Development and validation (author, year)	Data for equation	Equation	Population in which the formula was validated	Reference method	R^2	SEE
Lean Soft Tissue						
Janmahasatian et al., 2005	BW, BMI	LST (M) = (9270 × BW (kg)) ÷ [6680 + (216 × BMI)]	Normal and overweight men and women	DXA	0.93	0.77
		LST (W) = (9270 × BW (kg)) ÷ [8780 + (244 × BMI)]				
Fat-free mass						
Li et al., 2019	Age, Ht, BW	FFM = −5.382 − 0.037 x Age (y) + 0.154 x Ht (m)) + 0.502 x BW;	Healthy men and women	DXA	0.78	2.77
Appendicular lean mass						
Kulkarni et al., 2013	BW, Ht, Age	ALM (M) (Kg) = −13.432 – (0.0445 × Age (y)) + (0.200 × BW) + (0.140 × Ht (cm))	Healthy men and women	DXA	0.78	1.28
	BW, Ht, Age	ALM (W) (Kg) = −9.852 – (0.028 × Age (y)) + (0.170 × BW) + (0.102 × Ht (cm))	Healthy men and women	DXA	0.82	1.05
Skeletal muscle mass						
Lee et al., 2000	BW, Ht, Age, G	SMM (kg) (M):0.244 x BW (kg) + 7.80 x Ht (m) - 0.098 x Age (y) + 6.6 x G (1 for M) + Race (-1.2 Asian, 1.4 for African American and 0 for white and Hispanic) - 3.3.	Normal and overweight subjects	MRI	0.86	2.80
		SMM (kg) (W):0.244 x BW (kg) + 7.80 x Ht (m) - 0.098 x Age (y) + 6.6 x G (0 for W) + Race (-1.2 Asian, 1.4 for African American and 0 for white and Hispanic) - 3.3.				

Age (y): years; ALM: appendicular lean mass; BMI: body mass index; BW: body weight; DXA: Dual-energy X-ray absorptiometry; FFM: fat free mass; G: gender; Ht: height; LST: lean soft tissue; M: male; SMM: skeletal muscle mass; MRI: magnetic resonance imaging; R^2: linear coefficient of determination; SEE: standard error of the estimate; W: women;

Table S2. Correlation between muscle mass estimation changes data with anthropometric data and serum creatinine changes in baseline and hospital discharge.

Anthropometric data			Lean soft tissue mass	Fat-free mass	Appendicular lean mass
			Δ %	Δ %	Δ %
Median arm circumference (cm)	r p value (n)	Δ %	-0.369 0.001 131	0.363 0.001 131	0.377 0.001 131
Calf circumference (cm)	r p value (n)	Δ %	-0.166 0.060 129	0.177 0.044 129	0.187 0.034 129
Serum creatinine (mg/dL)	r p value (n)	Δ %	0.120 0.196 117	-0.131 0.159 117	-0.119 0.200 117

*Statistically significant p-value ($p<0.05$). Spearman Correlations.

Table S3. Sensitivity correlation between muscle mass estimation changes data with anthropometric data and serum creatinine changes in baseline and hospital discharge.

Anthropometric data			Lean soft tissue mass	Fat-free mass	Appendicular lean mass
			Δ %	Δ %	Δ %
Median arm circumference (cm)[1]	**r** **p value** **(n)**	Δ %	-0.466 0.009 30	0.463 0.010 30	0.463 0.010 30
Calf circumference (cm)[2]	**r** **p value** **(n)**	Δ %	-0.552 0.051 13	0.459 0.114 13	0.515 0.071 13
Serum creatinine (mg/dL)[3]	**r** **p value** **(n)**	Δ %	0.150 0.132 102	-0.173 0.083 102	-0.164 0.099 102

*Statistically significant p-value ($p<0.05$). [1]Patients without upper limb edema; [2]Patients without lower limb edema; [3]Patients without kidney disease; [a]Spearman correlation; r = correlation coefficient; n = number of individuals in the analysis. Spearman Correlations.

Table S4. Correlation between the median of energy and protein balance and consumption and the changes in muscle mass.

Balance and consumption		Lean soft tissue mass		Fat-free mass		Appendicular lean mass	
		Δ BRUTO	Δ %	Δ BRUTO	Δ %	Δ BRUTO	Δ %
Intake							
Calories (kcal/day)	**r** **p value** **(n)**	0.131 0.101 158	0.134 0.093 158	-0.109 0.173 158	-0.105 0.190 158	-0.125 0.118 158	-0.129 0.106 158
Calories (% of prescription)	**r** **p value** **(n)**	0.014 0.863 156	0.015 0.848 156	0.006 0.938 156	0.009 0.912 156	-0.004 0.961 156	-0.008 0.924 156
Protein (g/day)	**r** **p value** **(n)**	0.129 0.108 157	0.133 0.098 157	-0.106 0.186 157	-0.101 0.208 157	-0.122 0.129 157	-0.127 0.114 157
Protein (% of prescription)	**r** **p value** **(n)**	0.022 0.789 156	0.023 0.778 156	-0.007 0.935 156	-0.004 0.961 156	-0.014 0.867 156	-0.015 0.850 156
Median balance intake							
Caloric balance (kcal/day)	**r** **p value** **(n)**	-0.074 0.361 155	-0.074 0.363 155	0.083 0.306 155	0.085 0.292 155	0.076 0.345 155	0.076 0.347 155
Caloric balance (%)	**r** **p value** **(n)**	-0.042 0.607 155	-0.040 0.625 155	0.056 0.491 155	0.059 0.463 155	0.045 0.580 155	0.042 0.601 155
Protein balance (g/day)	**r** **p value** **(n)**	-0.099 0.224 154	-0.099 0.220 154	0.108 0.181 154	0.110 0.181 154	0.106 0.191 154	0.109 0.178 154
Protein balance (%)	**r** **p value** **(n)**	-0.065 0.425 154	-0.064 0.432 154	0.077 0.342 154	0.080 0.323 154	0.069 0.395 154	0.069 0.395 154

*Statistically significant p-value ($p<0.05$). r = correlation coefficient; n = number of individuals in the analysis.

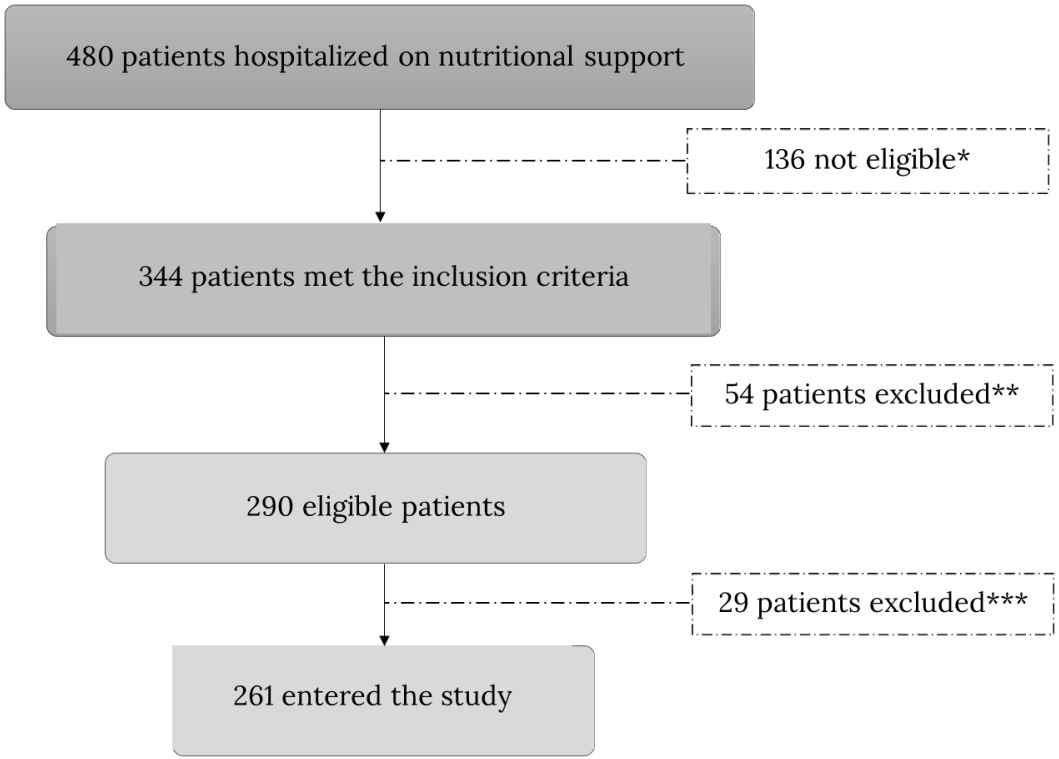
Table S5. Correlation between the clinical outcomes and the changes in muscle mass.

Clinical outcomes		Lean Soft Tissue		Fat-free mass		Appendicular lean mass	
		Δ BRUTO	Δ %	Δ BRUTO	Δ %	Δ BRUTO	Δ %
Total length of hospital staying	**r** **p value** **(n)**	0.141 0.077 157	0.139 0.082 157	-0.102 0.204 157	-0.098 0.222 157	-0.105 0.193 157	-0.103 0.198 157
Length of hospital staying with nutritional support	**r** **p value** **(n)**	0.151 0.059 158	0.152 0.057 158	-0.110 0.167 158	-0.105 0.189 158	-0.121 0.130 158	-0.121 0.131 158
Total complications	**r** **p value** **(n)**	0.126 0.116 158	0.129 0.106 158	**-0.171** **0.032** **158**	**-0.169** **0.034** **158**	**-0.179** **0.025** **158**	**-0.181** **0.023** **158**
Complications related to nutritional support	**r** **p value** **(n)**	0.154 0.054 158	0.155 0.051 158	**-0.183** **0.021** **158**	**-0.182** **0.022** **158**	**-0.191** **0.016** **158**	**-0.195** **0.014** **158**
Metabolic complications	**r** **p value** **(n)**	**0.245** **0.002** **158**	**0.245** **0.002** **158**	**-0.220** **0.005** **158**	**-0.219** **0.006** **158**	**-0.223** **0.005** **158**	**-0.227** **0.004** **158**
Infectious complications	**r** **p value** **(n)**	0.093 0.244 158	0.097 0.226 158	-0.106 0.187 158	-0.105 0.189 158	-0.113 0.157 158	-0.121 0.128 158
Reasons for interruption							
Foreseen reasons	**r** **p value** **(n)**	0.114 0.152 158	0.114 0.153 158	-0.151 0.059 158	-0.151 0.058 158	-0.158 0.048 158	-0.150 0.060 158
Unforeseen reasons	**r** **p value** **(n)**	0.026 0.749 158	0.028 0.723 158	-0.037 0.648 158	-0.031 0.695 158	-0.043 0.593 158	-0.042 0.600 158

*Statistically significant p-value ($p<0.05$). r = correlation coefficient; n = number of individuals in the analysis.

Figures

Figure S1. Patient flowchart.



*Patients ineligible who received only oral nutritional therapy and pediatric patients;
** Patients excluded due to refusal or discharge/death before signing the informed consent form;
*** Patients excluded for presenting only ideal weight data or the absence of anthropometric/nutritional data.

5.2. Artigo Original 2

Title:

"Association of adequacy and intake of calories and protein with clinical outcomes of patients using nutritional support: prospective study"

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Conflicts of interest
None declared.

Abstract

Background & Aims: An appropriate offering of nutrients ensures an adequate nutritional intake and during hospitalization, most patients at risk of malnutrition consume less than 75% of their daily needs. Suspension of the diet, and clinical complications, can deprive the patient of adequate nutrients. The present study aimed to evaluate the association of the consumption of calories and proteins with the clinical outcomes of patients admitted to a public hospital in Belo Horizonte, MG. **Methods:** A prospective observational study with patients over 18 years in use of enteral (EN) and/or parenteral nutritional (PN) therapy and monitored by the Nutritional Therapy Committee between December 14, 2021 and May 14, 2023. Data were collected from the electronic records and the exposure of interest was the EN and/or PN intake evaluated as protein and calorie per kilo (Kcal/Kg and g/Kg) and adequacy of intake (%). The data were presented as tertiles. The primary outcomes were death rate, length of hospital staying (LOS), length of hospital staying using nutritional support (LOSNS), interval between hospitalization and beginning of use of nutritional support. Secondary outcomes were the number of complications per day of hospitalization using nutritional support. **Results:** A total of 300 hospitalized patients using nutritional support were included in the study with a median of 61.5 (51–72) years old, 126 were women (42%). The median of LOSNS was 22 days and the median calorie intake per kg of body weight was 20.0 kcal (15.7–24.4), and the median protein intake per kg was 1.0 gram (0.9–1.2). Regarding intake adequacy (%), the median was 75.8% (58.0–87.0) for caloric adequacy and 71.6% (51.2–86.9) for protein adequacy. The mortality rate was 30.3% and gastrointestinal complications were the most frequent (81%). Patients in the 3rd tertile, with higher caloric and protein infusion, were associated with higher LOS and LOSNS, higher rates of mechanical complications, and lower rates of gastrointestinal complications. Furthermore, a higher protein intake in grams per kg was protective for death and was a predictor of the risk of referral to the ICU (p=0.014). **Conclusion:** Greater adequacy of intake was predictive of longer hospital stay. Protein intake was a protective factor against mortality and risk of referral to the ICU of patients using nutritional support during hospitalization. These findings reinforce the need for protocols to ensure adequate nutritional intake that minimize complications and prevent malnutrition.

Keywords: Nutritional Support. Adequacy. Caloric intake. Protein intake. Complications. Mortality.

Introduction

Hospital malnutrition has a high prevalence worldwide, affecting approximately 20%–50% of patients and leading to serious health consequences (1,2,3). Despite its multifactorial etiology, the main modifiable cause of hospital malnutrition is inadequate dietary intake (4). Studies show that reduced energy intake, combined with increased nutritional needs due to the disease process or treatment, is associated with increased clinical complications, morbidity, and mortality (5,6).

Through nutritional assessment, it is possible to determine nutritional status and design an individualized nutritional intervention (7). Nutritional needs should be established specifically according to body composition, disease, clinical and metabolic conditions, psychological and physical factors, as well as appetite (8). Thus, an appropriate offering of nutrients ensures an adequate nutritional intake (8). During hospitalization, most patients at risk of malnutrition consume less than 75% of their daily needs (9). In this context, intake deficits compromise nutritional status and can impair performance, quality of life, and survival. Therefore, nutritional support (enteral and/or parenteral nutrition) emerges as an auxiliary strategy to maintain nutritional status and meet the energy and protein needs of patients with different pathologies (10).

Despite its benefits, enteral nutritional feeding (EN) and parenteral nutrition (PN) present some negative consequences, such as metabolic, mechanical, and gastrointestinal impacts (11). Recent literature data show that suspension of the diet due to various problems and clinical complications, as well as the late introduction of nutritional support, can deprive the patient of adequate nutrients, neglecting the benefits of nutritional treatment (12). According to a prospective study carried out with more than 3,300 malnourished and critical patients, in 201 hospital units of 26 countries, 74.0% of hospitalized patients did not reach 80% of the energy goals and received only 61.2% of the calories and 57.6% of the prescribed proteins (13). In a longitudinal study of patients at a public hospital in Italy receiving PN, insufficient nutrients were provided to meet the patients' needs, with a median deficiency of 3.1 calories and 0.23 g of protein per kilogram of ideal body weight per day (14).

However, there is a knowledge gap in the subject, as most of these studies assessed consumption at a single time point, which is usually at the end of hospitalization, and it does not reliably represent patients' total consumption of during hospitalization. Thus, the present study considers the caloric and protein intake throughout the hospitalization period in patients receiving nutritional support.

In view of the above, the hypothesis for this study is that patients receiving nutritional support are receiving an insufficient supply of calories and proteins throughout the entire

hospitalization period, which can be associated with clinical complications. Therefore, the objective of the present study was to evaluate the association of the consumption of calories and proteins with the clinical outcomes of patients admitted to a public hospital in Belo Horizonte, MG.

Methods

This is a prospective observational study conducted at Hospital das Clínicas of the Universidade Federal de Minas Gerais, Brazil. All collected data were secondary information obtained from the electronic medical records of patients hospitalized between December 14, 2021 and May 14, 2023. The research was only started after approval by the Ethics Committee of the same university (CAAE 7966620.4.0000.5149).

Population

Participants were required to meet the following criteria for inclusion in the study: individuals aged 18 years or older, of both sexes, admitted by the Nutritional Support Commission and who had used EN and/or PN for at least 24 hours, associated or not with oral intake. Furthermore, patients must have signed the Free and Informed Consent Form. The following were excluded: patients who received only oral nutritional therapy, pediatric patients, pregnant women, patients/guardians who refused to sign the Informed Consent Form, and patients without measurements or with only ideal body weight data available. Patients who were previously enrolled in the project but who were subsequently readmitted to the hospital were also excluded.

Eligible participants were informed about the survey competencies. The use of accessible language and the resolution of doubts were based on the morality and confidentiality of information recommended by the Guidelines and Regulatory Norms for Research Involving Human Beings of the National Health Council (15). All participants and/or guardians who agreed to participate in the project signed the Free and Informed Consent Form, and data were only collected after this step.

Sample size calculation

Sample size calculation was performed based on the study of Lupián-Angulo and collaborators for the association between the use of nutritional therapy and complications (16). In this study, a difference of 11 days was observed in the length of stay of patients who received more than 80% of their energy needs compared to those who received less than 80% of their energy needs. Based on these differences, 78 patients would be needed, considering a power of 80%

and an alpha = 0.05. The average monthly flow of patients using nutritional support at the hospital in question is 20 patients.

Data collection

Data collection was conducted daily, apart from weekends, by a team of trained researchers, including students, professors, and professionals from the hospital. To identify eligible patients, the map of patients using enteral and parenteral diets generated daily by the Nutritional Therapy Commission of the hospital was consulted. After patients were identified and signed the Informed Consent Form, the researchers collected data from clinical and electronic records. No data were requested directly from the patients, their companions, or the professionals who followed them. The information collected by means of an electronic form in Google Docs®, and after the form was filled out, the data were processed in a database in the Microsoft® Excel program.

Nutritional data

All the nutritional evaluations were conducted by the hospitals' nutritionists, and the data were collected from the records. Anthropometric data included weight (kg), height (cm), body mass index (BMI) (kg/m²), and nutritional diagnosis. Weight and height were used if they were disclosed, measured, or estimated (17). If a patient's hospital record only had an entry for ideal body weight, that patient was excluded from the sample. BMI was calculated and grouped into five categories according to its classification (18) for adults and the elderly. The categories were underweight, adequate weight/eutrophy, overweight, and obesity. The nutritional diagnosis, on the other hand, showed great variability, so it was also grouped to facilitate understanding. The categories were suspected malnutrition; moderate malnutrition (including mild malnutrition and malnutrition); severe malnutrition; eutrophy; and overweight (assuming overweight and obesity as one category). These data are representative of the first nutritional assessment of these patients when they started nutritional support.

The exposure of interest was the EN and/or PN intake evaluated as protein and calories per kilo (kcal/kg and g/kg) and adequacy of intake (%). Intake was calculated as the median infusion estimated using the sum of energy or protein values available in the medical records, divided by the number of days with these data and divided by the mean body weight during the hospital stay. Adequacy was calculated as the percentage ratio of the median amount infused to that prescribed. Days without diet infusion, i.e., due to fasting, were included and counted as 0% adequacy. Patients without information on consumption were excluded from the analyses.

The intake and the adequacy of calories and protein were also presented as tertiles. Division of tertiles was conducted by recoding the variables in the statistical software;

therefore, the selection of groups and values was performed automatically, where the number of groups was determined (three tertiles). Patients were grouped according to consumption of kilocalories and grams per kilogram, as well as by caloric and protein adequacy in %, into three groups based on the classification by tertiles. The first tertile (1st) was considered low consumption/adequacy, the second tertile (2nd) as moderate, and the third tertile (3rd) as high consumption/adequacy.

Clinical data

The following data were collected from the electronic records: (1) demographic data (gender, age, race/color, date of birth, location); (2) hospitalization data (date of hospitalization, hospitalization sector, date of initiation of nutritional support, presence of neoplasm, performing dialysis, transfer to intensive care and palliative care); and (3) clinical outcomes.

The primary outcomes were clinical end points, including the death rate (%), length of hospital stay (LOS) (days), length of hospital stay using nutritional support (LOSNS) (days), and the interval between hospitalization and initiation of nutritional support (days). The secondary outcome was the number of complications per day of hospitalization using nutritional support. Complications related to nutritional support included metabolic complications (including hyper- and hypoglycemia, hyper- and hypokalemia, hyper- and hypophosphatemia, hyper- and hyponatremia, and hypertriglyceridemia); gastrointestinal complications (such as constipation, diarrhea, bloating, gastric residual volume, steatosis, cholelithiasis, gastroparesis, nausea, and vomiting); mechanical complications (tube exteriorization and obstruction); respiratory complications (aspiration, pneumothorax, and bronchoaspiration); and infectious complications (fever). Complications were analyzed as absolute frequency and in the form of occurrence rates, calculated as the total number of occurrences of the complication divided by the days of LOSNS.

It should be noted that the data on transfer to the ICU refers to those cases in which, during LOSNS, the patient stayed in an ICU bed. In this situation, those already admitted to the ICU were excluded from the analysis of this variable.

Statistical analysis

All data were arranged in an Excel® spreadsheet database and subsequently transferred to the statistical software Statistical Package for Social Sciences (SPSS®) version 20.0 (Chicago, IL, USA). There was a confidence interval of 95% and a significance level of $p<0.05$ to rejecting the null hypothesis.

Continuous variables were tested for normality using the Shapiro-Wilk test, and distribution was asymmetrical for all variables. Quantitative variables were described as

median (interquartile range (IQR) – P25 to P75). Categorical variables were described in absolute and relative frequency. Correlation analysis was performed using the Spearman test, to verify the association of caloric and protein intake(/Kg) and adequacy (%). Correlations were considered direct when they presented a positive correlation coefficient, and indirect when the coefficient was negative. Correlations were weak when the coefficient of correlation was <0.300, moderate, if coefficient between 0.300 and 0.500, and strong if >0.500 (19).

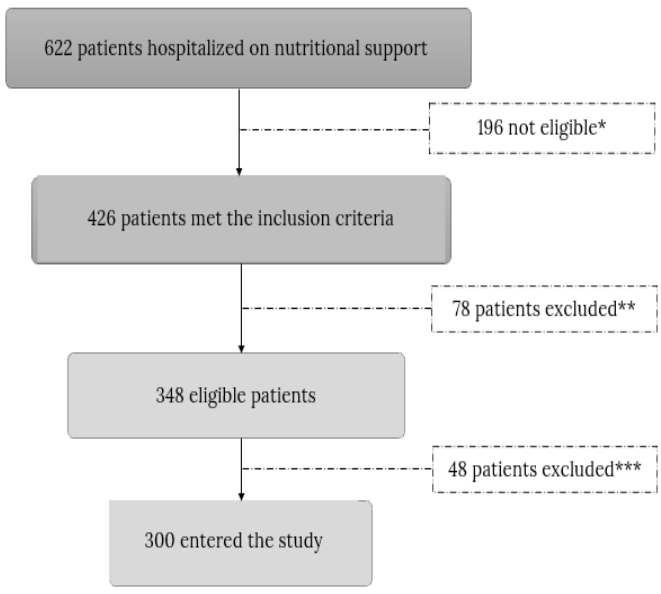
For the analyses, data on consumption of kcal and grams per kg and caloric and protein adequacy in % of patients grouped by classification of tertiles were used. For independent samples, the Kruskal-Wallis test was used to compare dietary and clinical aspects during hospitalization, considering ranges of caloric and protein adequacy. And for consumption per kilogram of weight, the same analysis was performed. The chi-square test was applied to the categorical variables like death, ICU admission and palliative care. The Dunn-Bonferroni test was performed to find the differences obtained when comparing the tertiles. Different letters represent statistical significance (P<0.05).

Finally, regression models were performed considering the three groups of adequacy of calorie and protein and the intake per Kg as independent variables. For linear regression models, the complication rates, LOS and LOSNS were used as dependent variables. The significance level adopted to enter the model was p<0.05, and the forward method was used. Binary logistic regression models were performed with death, palliative care or transfer to intensive care as dependent variables. For this last variable, the regression models were constructed excluding a variable sector, therefore only age and sex were included as adjustments.

Results

During the follow-up, 426 patients met the inclusion criteria, of which 300 hospitalized patients receiving nutritional support were included in the study (**Figure 1**).

Figure 1. Flowchart of patients in the study.



*Patients ineligible who received only oral nutritional therapy and pediatric patients;
** Patients excluded due to refusal or discharge/death before signing the informed consent form;
*** Patients excluded for presenting only ideal weight data or the absence of anthropometric/nutritional data.

Of those, 126 were women (42%) and 174 were men (58%), with a median age of 61.5 (51–72) years. Most patients were admitted to the clinical hospitalization wards (74.7%), and the others were in the ICU. Neoplasm was present in 126 patients (42%), and 42 (14%) were in palliative care, also, the same number (14%) underwent dialysis during their stay in the hospital when using nutritional support (**Table 1**).

As for nutritional status, the BMI of the patients ranged from 12.0 to 45.4 kg/m² with a median of 22.6 (19.0–26.0) kg/m², and the majority were classified as eutrophic (40.7%), followed by underweight (35.6%). According to the nutritional diagnosis given by the institution's protocol, severe malnutrition was the most prevalent (41.5%), followed by moderate malnutrition (20.4%). Exclusive EN was the main nutritional therapy instituted for most patients (73.3%), followed by EN associated with oral intake (14.3%), exclusive PN (9.4%), and finally PN with oral intake (3%). The most common type of enteral formula offered at the hospital was the high-protein formula (51.3%), which is also characterized as a high-energy (1.5 kcal/ml) and polymeric formula.

The median caloric intake per kilogram of body weight was 20.0 kcal (15.7–24.4), and the median protein intake per kilogram was 1.0 g (0.9–1.2). Regarding intake adequacy (%), the median was 75.8% (58.0–87.0) for caloric adequacy and 71.6% (51.2–86.9) for protein adequacy.

Table 1. General characteristics of the total sample.

Variables	**N (%)**
Age (years)	61.50 (51 - 72)
Gender	
Female (%)	126 (42)
Male (%)	174 (58)
Ethnicity	
White (%)	282 (94.1)
Other (%)	18 (5.9)
Hospitalization sector	
Intensive care unit (%)	76 (25.3)

Clinical admission (%)	224 (74.7)
Palliative care patients (%)	42 (14)
Cancer patients (%)	126 (42)
Dialysis patients (%)	42 (14)
Type of nutritional therapy	
Enteral nutrition (%)	220 (73.3)
Parenteral nutrition (%)	28 (9.4)
Enteral and oral nutrition (%)	43 (14.3)
Parenteral and oral nutrition (%)	9 (3)
Type of formulas offered	
Standard (%)	130 (43.3)
Hyperproteic (%)	154 (51.3)
Hypercaloric (%)	6 (2)
For diabetics (%)	5 (1.7)
For dialytic kidney disease (%)	5 (1.7)
Body mass index (Kg/m²)	
Underweight (%)	105 (35.6)
Healthy weight (%)	120 (40.7)
Overweight (%)	52 (17.6)
Obese (%)	18 (6.1)
Nutritional Diagnosis	
Suspected Malnutrition (%)	32 (10.7)
Moderate Malnutrition (%)	61 (20.4)
Severe malnutrition (%)	124 (41.5)
Eutrophy (%)	59 (19.7)
Overweight (%)	23 (7.7)

Data presented as median and interquartile interval or number and percentage.

Regarding the clinical outcomes, the median of LOSNS was 22 days, the mortality rate was 30.3%, and the percentage of patients referred to the ICU during hospitalization was 34.4%. Gastrointestinal complications were the most frequent (81%), followed by metabolic ones (70.7%). The median rates of clinical outcomes are presented in **Table 2**. It is important

to highlight that the crude rates of occurrence of some of the outcomes were presented due to the low rate of events in the sample. Therefore, the table includes the median number of events per patient and the median of the rate of events per days of hospitalization using nutritional support.

Table 2. Rates of clinical outcomes.

Variables	Data
Death Rate (%)	91 (30.3)
Transfer to ICU (%)	77 (34.4)
Total Hospitalization Time (days)	33 (22 - 50.75)
Length of Stay at the Support (days)	22 (11.25 - 35.75)
Frequency of events	
Metabolic complications (%)	212 (70.7)
Gastrointestinal complications (%)	243 (81)
Mechanical complications (%)	105 (35)
Infectious complications (%)	46 (15.3)
Respiratory complications (%)	2 (0.8)
Median of events / rate of events per hospital staying using nutritional support	
Complications related to nutritional support**	9.000 (4.000 -18.750) / 0.486 (0.191-0.868)
Metabolic complications**	2.500 (0.000-9.000) / 0.125 (0.000-0.379)
Gastrointestinal complications**	4.000 (1.000- 7.000) / 0.167 (0.049-0.0363)
Mechanical complications**	0.000 (0.000-1.000) / 0.000 (0.000-0.045)
Infectious complications**	0.000 (0.000-0.000) / 0.000 (0.000-0.000)
Respiratory complications**	0.000 (0.000-0.000) / 0.000 (0.000-0.000)
General complications **	10.000 (4.000-21.000) / 0.500 (0.215-0.966)

Data presented as median and interquartile interval or number and percentage. ** Rate of events by total days using nutritional support.

The caloric and protein intake and adequacy were each divided into tertiles: low (1st tertile), moderate (2nd tertile), and high (3rd tertile) (**Table 3**).

Table 3. Tertiles of consumption and adequacy.

Caloric intake (kcal/kg)		
1st tertile (n=100)	2nd tertile (n=104)	3rd tertile (n=96)
≤17.27	17.27 - 23.30	≥23.01
Protein intake (g/kg)		
1st tertile (n=187)	2nd tertile (n=17)	3rd tertile (n=96)
≤1.00	1.01 - 1.06	≥1.07
Adequacy of Calories (%)		
1st tertile (n=103)	2nd tertile (n=98)	3rd tertile (n=99)
≤64.00	64.01 - 83.00	≥83.01
Adequacy of Protein (%)		
1st tertile (n=100)	2nd tertile (n=100)	3rd tertile (n=100)
≤58.87	58.88 - 81.40	≥81.41

1st= first; 2nd = second; 3rd= third.

Patients in the 3rd tertile of caloric and protein adequacy (%) and intake (kcal/kg and g/kg) had longer LOS and LOSNS. Also, it was observed that patients in the 3rd tertile of caloric adequacy (%) had more mechanical complications. The post hoc, Dunn-Bonferroni test, showed that a difference was found between the 3rd tertile compared to the 1st tertile (45 vs 15, p=0.025). The same occurred for protein adequacy (%), patients with high adequacy had more mechanical complications (47 vs 22, p=0.004) than those with low protein adequacy. The difference was found between the 3rd tertile compared to 1st tertile. The death rates, indications for palliative care, and transfer to ICU were also compared among the tertiles. The patients in the 1st tertile of protein intake (in g/kg) had a higher incidence of referral to the ICU compared to the other groups (p = 0.014). No significant associations were observed for the other evaluated outcomes. Data shown in **table 4**.

Table 4. Clinical outcomes data according to caloric and protein intake or adequacy categories.

Clinical outcomes	Tertiles of adequacy and Intake															
	Calories (kcal/kg)				Calories (%)				Protein (g/kg)				Protein (%)			
	1st tertile (100)	2nd tertile (104)	3rd tertile (96)	P value	1st tertile (103)	2nd tertile (98)	3rd tertile (99)	P value	1st tertile (187)	2nd tertile (17)	3rd tertile (96)	P value	1st tertile (100)	2nd tertile (100)	3rd tertile (100)	P value
Total length of hospital staying (days)	28.00 (17.25 - 41.75)[a]	32.00 (21.00 - 46.25)[a]	40.50 (26.25 - 60.75)[b]	**<0.001**	15.00 (25.00 - 42.00)[a]	32.00 (21.00 - 45.25)[a]	41.00 (27.00 - 63.00)[b]	**<0.001**	21.00 (31.00 - 46.00)[a]	28.00 (17.50 - 40.00)[ab]	38.00 (25.00 - 61.75)[b]	**0.013**	27.50 (15.00 - 42.75)[a]	28.00 (20.25 - 41.75)[a]	43.00 (28.00 - 66.00)[b]	**<0.001**
Length of hospital staying with nutritional support (days)	16.00 (8.00 - 28.00)[a]	20.50 (12.00 - 33.00)[a]	31.00 (18.00 - 45.00)[b]	**<0.001**	15.00 (8.00 - 28.00)[a]	18.50 (10.75 - 33.50)[a]	31.00 (20.00 - 48.00)[b]	**<0.001**	20.00 (11.00 - 32.00)[a]	19.00 (10.50 - 34.00)[ab]	26.00 (15.50 - 44.75)[b]	**0.012**	16.00 (8.00 - 28.75)[a]	18.00 (10.25 - 31.25)[a]	31.00 (20.00 - 48.75)[b]	**<0.001**
Mechanical complications*	0.00 (0.00-0.029)	0.00 (0.00-0.056)	0.00 (0.00-0.049)	0.191	0.00 (0.00 - 0.00)[a]	0.00 (0.00 - 0.063)[ab]	0.00 (0.00 - 0.053)[b]	**0.025**	0.00 (0.00 - 0.042)	0.00 (0.00 - 0.059)	0.00 (0.00 - 0.046)	0.833	0.09 (0.00 - 036)[a]	0.14 (0.00 - 0.40)[ab]	0.19 (0.00 - 0.39)[b]	**0.004**
Palliative care**	13 (13%)	13 (12.5%)	16 (16.7%)	0.656	14 (13.6%)	14 (14.3%)	14 (14.1%)	0.989	29 (15.5%)	1 (5.9%)	12 (12.5%)	0.481	14 (14%)	14 (14%)	14 (14%)	1.000
ICU referral**	48 (48%)	43 (41.3%)	45 (46.9%)	0.593	45 (43.7%)	43 (43.9%)	48 (48.5%)	0.743	81 (43.3%)	3 (17.6%)	52 (54.2%)	**0.014**	46 (46%)	39 (39%)	51 (51%)	0.231
Death**	38 (38%)	27 (26%)	26 (27.1%)	0.122	36 (35%)	28 (28.6%)	27 (27.3%)	0.444	66 (35.3%)	4 (23.5%)	21 (21.9%)	0.055	33 (33%)	28 (28%)	30 (30%)	0.741

Data presented as median and interquartile range or mean ± standard deviation. * Median rate of events by length of hospital staying with nutritional support. Kruskal-Wallis Test.**Chi square Test. Different letters ([a],[b]) represent statistical significance (P<0.05).

Linear regression analyses using the univariate model were performed to understand the determinants of length of stay and clinical complications (**Table 5**). The dependent variables were clinical complication rates, LOS or LOSNS. Total LOS and LOSNS were positively associated with all independent variables of intake and adequacy (3rd tertile), both caloric and protein, in all models, including the unadjusted

model. Therefore, the greater the adequacy of intake and consumption per kilogram, the greater the LOS and LOSNS. For the outcome variable LOSNS (days), the 2nd tertile of caloric intake (kcal/kg) as an independent variable was also associated (data not shown). The infectious and respiratory complications did not show a significant association in any model with any independent variable of ingestion or consumption. Gastrointestinal complications were also associated with all independent variables of intake and adequacy, in all models. In addition, mechanical complications were positively associated with protein adequacy, in all four models, that is, the null model and in the models with adjustments.

Table 5. Regression models for clinical outcomes according to consumption and adequacy of protein and calories in tertiles.

Dependent variables	Null Models			Adjusted Models[1]			Adjusted Models[2]			Adjusted Models[3]		
	β	95%CI	p value	β	95%CI	p value	β	95%CI	p value	β	95%CI	p value
Adequacy of Calories (%) (independent variable)												
Length of hospital staying with nutritional support (days)	16.51	10.39-22.64	<0.001	16.16	10.02-22.31	<0.001	15.93	9.79-22.07	<0.001	15.70	9.55-21.84	<0.001
Total length of hospital staying (days)	18.81	11.12-26.50	<0.001	18.13	10.44-25.82	<0.001	17.87	10.18-25.56	<0.001	17.70	9.99-25.40	<0.001
Gastrointestinal complications	-0.123	-0.221--0.026	0.013	-0.129	-0.227--0.032	0.010	-0.136	-0.233--0.039	0.006	-0.137	-0.234--0.040	0.006
Adequacy of Protein (%) (independent variable)												
Length of hospital staying with nutritional support (days)	15.50	9.32-21.68	<0.001	15.29	9.11-21.47	<0.001	15.08	8.89-21.26	<0.001	14.94	8.77-21.11	<0.001
Total length of hospital staying (days)	17.89	10.17-25.60	<0.001	17.50	9.82-25.19	<0.001	17.29	9.59-24.98	<0.001	17.18	9.48-24.88	<0.001
Gastrointestinal complications	-0.109	-0.207-	0.029	-0.112	-0.210-	0.025	-0.119	-0.216-	0.017	-0.119	-0.217-	0.017

		-0.011			-0.014			-0.022			-0.022	
Mechanical complications	0.015	0.00-0.03	0.045	0.016	0.001-0.030	0.035	0.016	0.002-0.031	0.030	0.017	0.002-0.031	0.026
Caloric intake (kcal/kg) (independent variable)												
Length of hospital staying with nutritional support (days)	16.32	10.07 - 22.57	<0.001	15.97	9.69 - 22.24	<0.001	16.06	9.82 - 22.31	<0.001	16.04	9.81 - 22.27	<0.001
Total length of hospital staying (days)	16.89	8.99 - 24.80	<0.001	16.21	8.32 - 24.11	<0.001	16.32	8.44 - 24.19	<0.001	16.30	8.42 - 24.17	<0.001
Gastrointestinal complications	-0.103	-0.21 – -0.004	0.041	-0.109	-0.21 - -0.009	0.032	-0.107	-0.21 – -0.008	0.034	-0.107	-0.21 – -0.008	0.034
Protein intake (g/kg) (independent variable)												
Length of hospital staying with nutritional support (days)	9.17	3.54 - 14.81	0.002	8.82	3.17 - 14.47	0.002	9.05	3.41 - 14.68	0.002	9.17	3.54 - 14.79	0.001
Total length of hospital staying (days)	11.37	4.34 - 18.39	0.002	10.23	3.71 - 17.74	0.003	10.97	3.96 - 17.98	0.002	11.07	4.06 - 18.08	0.002
Gastrointestinal complications	-0.091	-0.179 - -0.004	0.040	-0.097	-0.184 - -0.009	0.031	-0.092	-0.178 - -0.005	0.038	-0.092	-0.178 - -0.005	0.039

Simple linear regression model. Data for 3rd tertile; 1st tertile as reference. Null Models: each variable was inserted in the linear regression analysis without the addition of any adjustment variable.
Adjusted Models¹: adjusted for age;
Adjusted Models²: adjusted for age and sector;
Adjusted Models³: adjusted for age, sector and sex.
CI, confidence interval; OR, odds ratio; - = non-significant data.

Binary logistic regression analysis was performed to understand how caloric and protein adequacy and intake (independent variables) determine the probability of death, palliative care, or transfer to the ICU (dependent variables). The results of this analysis are presented in **Table 6**. According to the analyses, the probability of death was reduced by 49% in the null model and 46% in the models with adjustments, for patients in the 3rd tertile compared to the 1st tertile of protein intake in grams per kilogram. An 82% increase in the odds of referral to the ICU was also

observed in model 2 and an 85% increase in risk in model 3 for patients in the 3rd tertile compared to the 1st tertile for the same independent variable of protein intake per kilogram. No significant association was found for palliative care as a dependent variable or for the other independent consumption and adequacy variables (data not shown).

Table 6. Logistic regression models for clinical outcomes according to consumption and adequacy of protein and calories in tertiles.

Dependent variables	Null Models			Adjusted Models¹			Adjusted Models²			Adjusted Models³		
	OR	95%CI	p value	OR	95%CI	p value	OR	95%CI	p value	OR	95%CI	p value
Protein intake (g/kg) (independent variable)												
ICU referral**	1.55	0.94 - 2.54	0.084	1.56	0.95 - 2.56	0.081	1.82	1.06- 3.11	0.030	1.85	1.07- 3.18	0.027
Death**	0.51	0.29- 0.91	0.022	0.54	0.30- 0.95	0.033	0.54	0.30- 0.97	0.038	0.54	0.30- 0.97	0.041

Binary logistic regression model. Data for 3rd tertile; 1st tertile as reference. Null Models: each variable was inserted in the logistic regression analysis without the addition of any adjustment variable.
Adjusted Models¹: adjusted for age;
Adjusted Models²: adjusted for age and sector;
Adjusted Models³: adjusted for age, sector and sex.
CI, confidence interval; OR, odds ratio;
- = non-significant data

Discussion

This study aimed to evaluate the association between intake and adequacy of energy and protein with clinical outcomes in patients using nutritional support. The results showed that higher caloric and protein infusion was associated with higher LOS and LOSNS, higher rates of mechanical complications, and lower rates of gastrointestinal complications. Furthermore, a higher protein intake in grams per kilogram was protective against death compared to a low intake. At the same time, the highest protein intake per kilogram was a predictor of the risk of referral to the ICU.

Establishing an adequate supply of calories and protein through nutritional support for patients is a challenge, since estimations of energy and macronutrient requirements are complex and variable (20). This problem promotes an inconsistent prescription of kilocalories and a consequent adequate delivery (21). In the literature, a low calorie and protein supply has been associated with longer LOS (ICU and total hospitalization) and lower hospital discharge rates (21, 22). However, the opposite was seen in our study, where greater adequacy of intake was related to greater LOS and LOSNS. One hypothesis that explains this finding is that patients who had a longer support period had a more effective progression of the volume of the diet and consequently, higher consumption. The study by Couto et al. (23) confirms this fact by reporting that the LOS interferes with the supply of energy, since patients with longer stays tend to achieve greater adequacy relative to the proposed calorie goal. The ASPEN recommendations suggest that nutrition should be progressed gradually to reach 50%–65% of caloric needs in the first 48–72 h of hospitalization, increasing over the course of days (24). Nevertheless, it should be taken into consideration that there are several factors that delay this progression, such as interruptions, complications, and even the patient's clinical condition. In this study, 25.3% of the sample was transferred to the ICU. These data suggest that the clinical condition of these patients was aggravated, and, consequently, because they required greater care, it is assumed that there was a greater decline in their general condition, culminating in damage to the supply of nutrients and compromising their nutritional status.

Another hypothesis that can be raised concerns the supply of calories and proteins. In the study by Yeh and collaborators (22) cited above, there was a reduction in LOS and LOSNS in patients with higher consumption; however, the initial targets for calories and proteins were already much higher than those found in our study. In our sample, even the patients who had higher caloric and protein intakes and an intake adequacy above 75% had a median of 20 kcal/kg and 1.0 g/kg. In general, it is noted that there was a low intake of calories and proteins, and therefore, it was not effective in reducing the aforementioned outcomes. It should be noted that in our study, that none of the patients were overfed (defined as energy intake >110% of

energy expenditure measured by calorimetry) but had an intake close to 100%, i.e., greater than 75%, but none had an intake greater than 100%.

A higher intake of calories and protein was associated with more mechanical complications. This group of complications comprises tube exteriorization and obstruction. In this study, about 35% of the sample had mechanical complications, the most common being tube exteriorization, with 190 cases of occurrence (32.3%). Some complications may occur shortly after tube placement, but others may develop later, especially in elderly patients with comorbidities and infections (25). Among the main causes of mechanical complications, poor positioning, inadequate insertion, displacement, and accidental removal/exteriorization of the tube have been cited (26). Blind insertion results in mispositioning in up to 16% of cases, which can result in serious complications. In a review by Sparks et al. (27), approximately 1.9% of probe placements were inappropriate, and misplacement accounted for 13%–32% of subsequent repositioning attempts. Another study demonstrated that of 932 blind attempts to place a post-pyloric tube, 433 (46%) failed (28). Unplanned removal of the feeding tube can be explained by reasons inherent to the patient, as it is an external agent, whose long stay time can cause discomfort (29). As it requires new insertion and the use of more material, it increases associated expenses, reinforcing the need for greater care by the health team (30). In this study, infusion of the diets of all patients was performed by an infusion pump. This may explain the lower incidence of cases of tube obstruction, as there is a greater periodicity of care.

Similar to the findings of this study, a meta-analysis of randomized controlled trials found that continuous feeding was associated with a reduced incidence of food intolerance (31). Therefore, food intolerance results from gastrointestinal complications and interferes with the provision of nutritional support. Thus, it seems certain that patients with greater intake adequacy had a lower incidence of gastrointestinal complications because they acquired greater tolerance to the infused volumes. The association of higher caloric and protein intake with a higher total complication rate seems to be more associated with the clinical severity of the patients than with the nutritional infusion itself, given that food intolerance is common during the acute phase of critical illness and can result in an inadequate supply of nutrients (32). This hypothesis is in line with the findings of a study by Heyland et al. (32), where the rate of EN food intolerance increased from 1% on day 1 to 6% on days 4 and 5 and decreased daily thereafter. Therefore, intolerance decreased as the diet progressed, and the severity of the disease was attenuated, corroborating our previously mentioned findings.

According to our results, higher protein intake was more strongly protective against mortality than lower intake. Our data contribute to the ongoing debate on this topic, as the existing literature presents controversial data. Protein intake was associated with a decreased

risk of mortality in some investigations, such as a prospective cohort study with 70,696 participants from Japan who had no history of cancer or heart disease (33). Another cohort study with elderly people demonstrated that a higher intake of vegetable protein was associated with a reduction in overall mortality in both sexes. Lower mortality was mainly attributed to plant proteins (34). The study by Chan et al. (35) demonstrated that men in the highest quintile of total protein intake had a reduction in mortality by 29% [95% CI: 0.55–0.92, p = 0.017] and 38% [95% CI: 0.39–0.97, p = 0.041] compared to lower quintiles. In Chan's study (35), the mean protein intake was 1.4 and 1.2 g/kg of body weight, respectively, for men and women, which reflects a higher protein intake when compared to the present study, whose median was 1.0 g/kg. Regarding hospitalized patients using nutritional support, two studies corroborated our findings, one of which was performed by Allingstrup et al. (36), who demonstrated that providing protein in the highest tertile (1.46 g/kg), compared to the lowest tertile (0.79 g/kg), was associated with lower ICU mortality. The second study, with 843 patients, showed that the intake of a higher amount of protein (≥1.2 g/kg/day) was associated with lower hospital mortality rates (OR: 0.42; 95% CI: 0. 21; 0.83; p = 0.013) in non-septic and non-overfed patients (37). A mechanism that could explain this association between protein intake and mortality is anabolic resistance to proteins during aging. With the consequent greater protein intake, there is a greater intake of amino acids such as leucine, which promotes anabolism, stimulating the activity of mTORC1 in older adults and cysteine, which from the synthesis of glutathione, counteracts the decline of age by combating the increase in the oxidative state and bringing benefits and greater longevity (35).

In this study, it was observed that a higher protein intake was a risk factor for referral to intensive care. A systematic review and meta-analysis of randomized clinical trials compared a high protein supply with a low supply in critically ill patients, and the authors concluded that higher protein levels were associated with a trend towards a shorter ICU stay (p = 0.13) (38). One hypothesis that explains this finding is the fact that certain clinical conditions, such as chronic inflammation and oxidative stress associated with metabolic impairment, are inherent characteristics of a patient who requires transfer to the ICU and, consequently, are factors that overshadow the benefits of higher protein intake in the organism (34).

It should also be considered that patients receiving nutritional support receive macronutrients in different ways, and the composition of the formulas are varied and may also have protein modules in the infusion. Therefore, protein sources, intake of other nutrients, and biological factors can also affect clinical outcomes (39).

Although this is a relevant and unique study on the subject, some limitations must be explored. First, it is an observational study using secondary data; therefore, all the information

used came from the professionals' medical records. This practice can allow systematic errors to occur and not be clearly detected. In addition, the sample, despite its robustness, is very heterogeneous. The patients had different pathologies and specific clinical conditions, which, when evaluated together, were not considered. Finally, quantifying the improvement in consumption is a complex task, as the patient sometimes received more than one type of nutrition, and this may have generated an overestimation of values. However, measures were taken to minimize confounding factors. The entire team underwent rigorous training before data collection, missing and conflicting information was checked in the system again, and the methodology was rigorous to obtain reliable results.

Conclusion

Considering the results from the present study, it can be inferred that there exists a significant correlation between the intakes and clinical outcomes of patients receiving nutritional support. Greater adequacy of caloric and protein intake was predictive of a longer hospital stay, but protective against gastrointestinal complications, although more mechanical complications may appear. Protein intake was a protective factor against mortality and risk for referral to the ICU for patients using nutritional support during hospitalization. Considering the findings of this study, the need to create effective protocols for the fulfillment of an adequate nutritional support, the minimization of complications related to EN and PN and the prevention of malnutrition is encouraged. Additional studies should be conducted to broaden the discussion about the importance of nutritional adequacy.

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5.3. Artigo Original 3

Title:

"Challenges of nutritional support administration and clinical outcomes during hospitalization: a prospective study"

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None declared.

Abstract

Background & Aims: Malnutrition is a public health problem with a high prevalence in hospitalized patients. Furthermore, dietary interruptions, the suspension of the diet and the late introduction of nutritional support can block adequate nutrients to offer, neglecting the benefits of nutritional treatment. The present study aimed to evaluate the administration of nutritional support and its clinical impacts in patients admitted to a public hospital in Belo Horizonte, MG.

Methods: A prospective observational study with secondary data obtained from the electronic medical records of patients hospitalized in use of enteral and/or parenteral nutritional therapy, between 14 December 2021 and 14 May 2023. The exposure variables were interval between hospitalization and beginning of use of nutritional support and number of diet interruption. The main outcome in this study was death rate, and secondary outcomes were ICU admission, length of hospital staying (LOS), length of hospital stay with nutritional support (LOSNS), risk of refeeding syndrome and presence of pressure injury.

Results: A total of 300 patients were included in the study, 174 were men (58%) and a median age of 61.50 years (51 – 72). 83.3% of patients started nutritional support in more than 48 hours. 71.7% of patients had their diet interrupted at some point during hospitalization. Late initiation of nutritional support was associated with higher mortality, longer LOS and lower risk of refeeding syndrome ($p<0.001$). The chances of death were increased in more than 30x in the models with adjustments for unexpected interruptions. Expected interruptions were associated with higher LOS ($p=0.001$), LOSNS ($p=0.001$), pressure injury ($p=0.042$) and increased the risk of refeeding syndrome by up to 29x.

Conclusion: About 2/3 of patients had at least one interruption of the diet infusion. Delayed initiation of nutritional support and dietary interruptions, even when expected, had a negative impact on patients' clinical outcomes. The data emphasize the importance of offering adequate intake to patients using nutritional support. And they reinforce the need to monitor hospital malnutrition and dietary infusion, in order to minimize health problems.

Keywords: Nutritional Support. Diet infusion. Interruptions of diet. Refeeding syndrome. Pressure injury.

Introduction

Malnutrition is a clinical condition resulting from nutrient imbalance that leads to adverse effects on body composition (1). It is a public health problem with a high prevalence in hospitalized patients, and it can be present on hospital admission, and it could also be developed during hospitalization (2). Multiple clinical conditions (polymorbidity) affect more than 70% of hospitalized adults and, when combined with age, it contributes to malnutrition and higher mortality (3). A prospective study demonstrated that having a high comorbidity index (greater than two) was a predictor of malnutrition at hospital admission (4).

Maintaining adequate nutrient intake in these patients is a crucial factor for minimizing the impacts of malnutrition on nutritional status and quality of life (5). However, studies report progressive malnutrition during hospitalization, caused in many cases due to inadequate nutritional intake (1). A recent Brazilian study with 295 elderly people revealed a prevalence of energy intake inadequacy around 96 % and 69 % for protein intake. It was found that these high rates have been associated with the pathogenesis of sarcopenia and cachexia, highlighting the importance of ensuring an adequate nutritional supply (6).

In order to prevent adverse effects associated with malnutrition, guidelines recommend starting nutritional support during hospitalization in clinical patients who are at risk of malnutrition (7). Early nutritional support (provided less than 48 hours after hospital admission) is indicated for hospitalized polymorbid patients (3), critically ill patients (8) and after surgery (9). Early nutritional support contribute to the reduction of lean mass loss, improves clinical results, in addition to prevent bacterial translocation and reducing hospitalization time (3,8).

However, among the obstacles to obtain an adequate supply of nutrients are dietary interruptions that limit the use of the complete supply of enteral (EN) and parenteral nutrition (PN), leading to inadequate energy and protein intake (10). In these cases, both the suspension of the diet and the late introduction of nutritional support can block adequate nutrients to offer, neglecting the benefits of nutritional treatment (11). A prospective study carried out with more than 3,300 malnourished and critically ill patients in 201 units in 26 countries, showed that, on average, 74.0% of hospitalized patients did not reach 80% of the energy goals and received only 61.2% of calories and 57 .6% of prescribed proteins (12). The same situation was observed in Brazil, where 6.5% of critically ill patients using EN meet 80% of their energy needs (13), while only 3.3% reached the protein target in 72h. Furthermore, the main reason for delaying the start of the diet or limiting its progression was gastrointestinal complications (13).

In view of the above, there is a gap in the literature regarding the impact of nutritional support administration challenges throughout the hospitalization period. Thus, the present study arises with the hypothesis that most patients are already admitted with malnutrition or at

nutritional risk in the hospital, and when this condition is associated with a late start of nutritional support, it leads to serious adverse effects, mainly due to frequent interruptions in the diet that limit the provision of adequate nutrition. Therefore, the objective of the present study was to evaluate the administration of nutritional support and its clinical impacts in patients admitted to a public hospital in Belo Horizonte, MG.

Methods

This is a prospective observational study carried out at Hospital das Clínicas of the Federal University of Minas Gerais, Brazil. All collected data were secondary information obtained from the electronic medical records of patients hospitalized between 14, December 2021 and 14, May 2023. The research was only started after approval by the Ethics Committee of the Federal University of Minas Gerais (CAAE 7966620.4.0000.5149).

Population

Participants were required to meet the following criteria for inclusion in the study: individuals aged 18 years or older, of both sexes, admitted by the Nutritional Support Commission and who had used EN and/or PN for at least 24 hours, associated or not with oral intake. Furthermore, patients must have signed the Free and Informed Consent Form. The following patients were excluded: patients who received only oral nutritional therapy, pediatric patients, pregnant women, patients/guardians who refused to sign the Informed Consent Form, and patients without measurements or with only ideal body weight available. Patients who were previously enrolled in the project but who were subsequently readmitted to the hospital were excluded.

Eligible participants were informed about the survey competencies. The use of accessible language and the resolution of doubts were based on the morality and secrecy of information recommended by the Guidelines and Regulatory Norms for Research Involving Human Beings of the National Health Council (14). All participants and/or guardians who agreed to participate in the project signed the Free and Informed Consent Form, with data being collected only after this step.

Sample size calculation

Sample size calculation was performed based on the study of Lupián-Angulo and collaborators on the association between the use of nutritional therapy and complications (15). In this study, a difference of 11 days was observed in the length of stay of patients who received more than 80% of their energy needs compared to those who received less than 80% of their energy

needs. Based on these differences, 78 patients would be needed, considering a power of 80% and an alpha = 0.05.

Data collection

The data collection was carried out daily, except for weekends, by a team of trained researchers, including graduations and post-graduation students, and professionals from the hospital. To identify eligible patients, the map of patients using enteral and parenteral diets generated daily by the Nutritional Therapy Commission of the hospital was consulted. After identifying and signing the Informed Consent Form, the researchers collected data from clinical and electronic records. No data was requested directly for the patient, their companion, or the professionals who followed them. The collected information was set in an electronic form on Google Docs®, and after filling it out, it was computed in a database in the Microsoft® Excel program.

Nutritional data

All the nutritional evaluations were carried out by the hospitals' nutritionists and the data collected from the records. Anthropometric data included weight (Kg), height (cm), Body mass index (BMI) (Kg/m²) and nutritional diagnosis. Weight and height were used if they were informed, measured, or estimated (16). If a patient had only a register of the ideal body weight on its hospital record, it was excluded from the sample. BMI was grouped into five categories according to its classification (17) for adults and the elderly. The categories were: underweight, adequate weight/eutrophy, overweight and obesity. The nutritional diagnosis, on the other hand, showed great variability, so it was also grouped to facilitate understanding. The categories were: suspected malnutrition; moderate malnutrition including mild malnutrition and malnutrition; severe malnutrition; eutrophy, which also includes patients with nutritional risk, and finally overweight, including overweight and obesity. These data are representative of the first nutritional assessment.

Clinical data

The following data were collected from the electronic records: (1) demographic data (gender, age, race/color, date of birth, location); (2) hospitalization data (registration number, date of hospitalization, bed, hospitalization sector, clinical comorbidities, past medical history, presence of neoplasm, performing dialysis, transfer to intensive care and palliative care); and (3) exposures variables and clinical outcomes.

The exposure variables analyzed were: interval between hospitalization and beginning of use of nutritional support (days); number of diet interruption and reasons for it, and

categorized into expected and unexpected interruptions. Interruptions were analyzed in the form of occurrence rates, calculated as the total number of the interruptions divided by the days of length of hospital staying using nutritional support (LOSNS). The expected reasons for interrupting the diet included breaks for procedures and exams, for monitoring of oral intake, due to lack of prescription or breaks for confirmation of catheter positioning. The unexpected reasons for interrupting the diet included interruptions due to hemodynamic instability, abdominal distention, stasis, diarrhea or vomiting, in addition to catheter exteriorization or obstruction.

The main outcome in this study was death rate (%), and secondary outcomes were ICU admission (%), length of hospital staying (LOS) (days), LOSNS (days); risk of refeeding syndrome and presence of pressure injury. The last two outcomes were analyzed as categorical variables, calculated as the number of patients with or without these conditions. It should be noted that the data on ICU admission refers to those cases in which, during LOSNS, the patient stayed in an ICU bed. In this situation, those already admitted to the ICU were excluded from the analysis.

Statistical analysis

All data were arranged in an Excel® spreadsheet database and subsequently transferred to the statistical software Statistical Package for Social Sciences (SPSS®) version 20.0 (Chicago, IL, USA). There was a confidence interval of 95% and a significance level of $p < 0.05$ to rejecting the null hypothesis.

Continuous variables were tested for normality using the Shapiro-Wilk test, and distribution was asymmetrical for all variables. Quantitative variables were described as median (interquartile range (IQR) – P25 to P75). Categorical variables were described in absolute and relative frequency.

Correlation analysis was performed using the Spearman test, to verify the association between exposure variables and clinical outcomes according to the interval between admission and the start of nutritional support. In addition, sensitivity correlations were made according to patients who received nutritional support within 48 hours or more. Correlations were considered direct when they presented a positive correlation coefficient, and indirect when the coefficient was negative. Correlations were weak when the coefficient of correlation was <0.300, moderate, if coefficient between 0.300 and 0.500, and strong if >0.500 (18).

For independent samples, the Mann-Whitney test was used to compare clinical outcomes data according to the interval between admission and the start of nutritional support (patients who received nutritional support within 48 hours or more). Mann-Whitney test was also performed to compare interruptions during hospitalization and the interval between

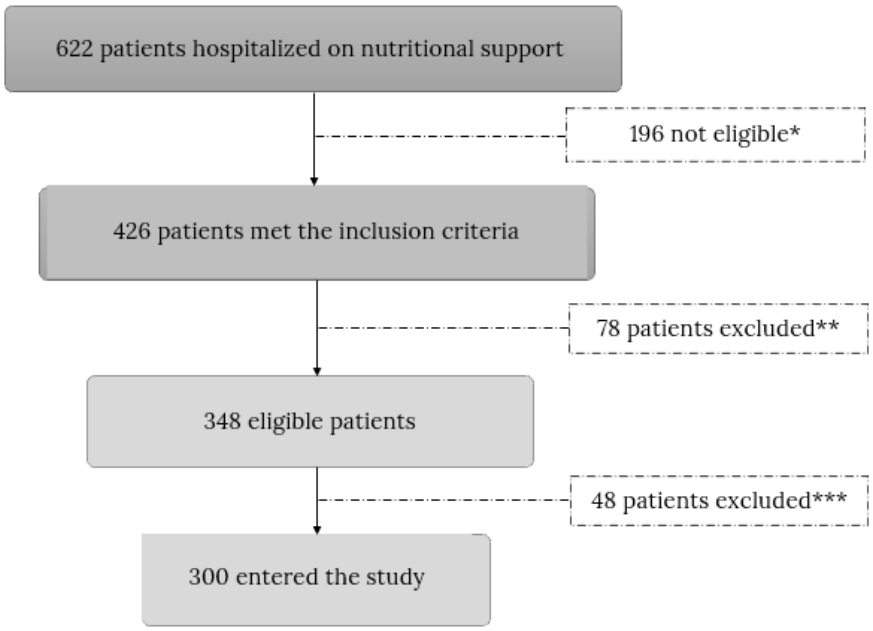
admission and the start of nutritional support, considering the group of patients who died and those who survived, those admitted to the ICU and not admitted during hospitalization as well as those who presented or not risk of refeeding syndrome and pressure injury. The chi-square test was applied to compare death, ICU admission and risk of refeeding syndrome and pressure injury according to the time when nutritional support started.

Regression models were performed considering the Interval between admission and the start of nutritional support, expected interruptions and unexpected interruptions as independent variables. For linear regression models, LOS and LOSNS were used as dependent variables. The significance level adopted to enter the model was $p<0.20$, and the forward method was used. Binary logistic regression models were performed with death, admission to intensive care, risk of refeeding syndrome and pressure injury as dependent variables.

Results

During the evaluation period, 426 patients met the study inclusion criteria, however 78 were excluded due to refusal or discharge/death before signing the Informed Consent Form. Thus, 348 were eligible, but 48 presented only ideal body weight data or the absence of anthropometric/nutritional data. Of these, 300 were included in the study (**Figure 1**).

Figure 1. Flowchart of patients in the study.



*Patients ineligible who received only oral nutritional therapy or pediatric patients; ** Patients excluded due to refusal or discharge/death before signing the informed consent form; *** Patients excluded for presenting only ideal weight data or the absence of anthropometric/nutritional data.

The sample consisted of a larger number of men 174 (58%) and sample presented a median age of 61.50 years (51 - 72). Most of the patients were admitted to the clinical admission sector (74.7%), mostly using exclusively enteral nutrition (73.3%). The highest prevalence of BMI classification was eutrophy (40.7%) followed by underweight (35.6%). And the most prevalent nutritional diagnosis was severe malnutrition (41.5%). The data is presented in **table 1**.

Table 1. General characteristics of the total sample.

Variables	**N (%)**
Age (years)	61.50 (51 - 72) *
Gender	
Female (%)	126 (42)
Male (%)	174 (58)
Ethnicity	
Black (%)	13 (4.3)
Other (%)	287 (95.7)
Hospitalization sector	
Intensive care unit (%)	76 (25.3)
Clinical admission (%)	224 (74.7)
Palliative care patients (%)	42 (14)
Cancer patients (%)	126 (42)
Dialysis patients (%)	42 (14)
Type of nutritional therapy	
Enteral nutrition (%)	220 (73.3)
Parenteral nutrition (%)	28 (9.4)
Enteral and oral nutrition (%)	43 (14.3)
Parenteral and oral nutrition (%)	9 (3)
Body mass index (Kg/m²)	
Underweight (%)	105 (35.6)
Healthy weight (%)	120 (40.7)
Overweight (%)	52 (17.6)

Obese (%)	18 (6.1)
Nutritional Diagnosis	
Suspected Malnutrition (%)	32 (10.7)
Moderate Malnutrition (%)	61 (20.4)
Severe malnutrition (%)	124 (41.5)
Eutrophy (%)	59 (19.7)
Overweight (%)	23 (7.7)

*Data presented as median (IQR).

Regarding the exposure variables studied, the median interval between admission and the start of nutritional support was 6 days. A total of 83.3% of patients started nutritional support in more than 48 hours. In addition, 71.7% of patients had their diet interrupted at some point during hospitalization, being most (54%) unexpected interruptions. More information is available in **table 2**.

Table 2. Occurrence rates of exposure variables.

Variables	**Data**		
Interval between admission and the start of nutritional support (days)	6 (4 - 13)		
Patients who started nutritional support within 48 hours (%)	50 (16.7)		
Patients who started nutritional support in more than 48 hours (%)	250 (83.3)		
	Number of patients with events	**Median of events per person**	**Rate of events for person[1]**
Total Diet infusion interruptions	215 (71.7)	2.0 (0.0-3.0)	0.1 (0.0-0.1)
Expected diet interruptions	144 (48)	0.0 (0.0-1.0)	0.0(0.0-0.1)
Unexpected diet interruptions	162 (54)	1.0 (0.0-2.0)	0.02 (0.00-0.08)

Data presented as number and percentage or median and interquartile interval. [1] Rate of events per hospital staying using nutritional support.

As for clinical outcomes, 34.4% required intensive care during hospitalization and 30.3% evolved to death. The median length of hospital stay was 33 days and the time spent receiving nutritional support was 22 days. Regarding secondary outcomes, 14% had pressure injury and 12% risk of refeeding syndrome. More details are present in **table 3**.

Table 3. Rates of clinical outcomes.

Outcomes	Data
Death Rate (%)	91 (30.3)
ICU admission (%)	77 (34.4)
Length of hospital Stay (days)	33 (22 - 50.75)
Length of Hospital Stay with Nutritional Support (days)	22 (11.25 - 35.75)
	Number of patients with events
Risk of refeeding syndrome (%)	36 (12)
Pressure injury (%)	42 (14)

Data presented as number and percentage or median and interquartile interval.

The occurrence of clinical outcomes was presented according to the interval between admission and the start of nutritional support (up to 48h versus more than 48h) and the data is available in **table 4**. Patients who started nutritional support in more than 48 hours had greater LOS compared to patients who started nutritional support within 48 hours ($p<0.001$). The opposite was seen for the risk of refeeding syndrome, where a greater number of patients presented risk of refeeding syndrome among those who started support within 48 hours compared to the incidence in the others ($p<0.001$). Patients who started nutritional support in more than 48 hours also had greater death rate, pressure injury and ICU admission rates compared to those who started nutritional support up to 48h of hospital admission, however, the findings were not statistically significant, as can be seen in **Table 4**.

Table 4. Clinical outcome data according to the interval between admission and the start of nutritional support.

OUTCOMES	EXPOSURE		
	Interval between admission and the start of nutritional support		
	≤ 48 hours (n=50)	> 48 hours (n=250)	P value
Length of hospital Stay (days)	24.5 (13.7 - 37.0)	34.0 (23.0 - 54.0)	**<0.001**
Length of Stay with nutritional support (days)	21 (11 - 34)	22 (12 - 37)	0.908
Risk of refeeding syndrome (%)*	14 (28%)	22 (8.8%)	**<0.001**

Pressure injury (%)*	6 (12%)	36 (14.4%)	0.655
Death (%)*	11 (22%)	80 (32%)	0.160
ICU admission (%)*	19 (38%)	117 (46.8%)	0.254

Data presented as median and interquartile interval. Mann Whitney U Test. *Chi square test.

The **table 5** presented the correlation between clinical outcomes and interval between admission and the start of nutritional support (more or within 48 hours), number of diet interruptions (expected and unexpected). Correlations with the entire sample (n=300), it was observed a direct and moderate correlation between the interval between admission and the start of nutritional support with LOS (p=0.001). Therefore, the longer the interval for starting nutritional support, the longer the hospital stay in the entire sample. The expected reasons for diet interruptions were directly and weakly correlated with all clinical outcomes, demonstrating that the more interruptions predicted in the diet infusion, the longer the LOS (p=0.001) and the longer the LOSNS (p=0.001). There was no significant correlation for unexpected reasons for diet interruptions.

Sensitivity correlations were performed between the same variables, separated by the interval between hospital admission until the start of nutritional support. Patients who started nutritional support within 48 hours did not show any significant correlation of exposure and clinical outcomes. For patients who started nutritional support in more than 48 hours, a direct and moderate correlation was seen between the interval between admission and the start of nutritional support with LOS (p=0.001). Expected reasons for diet interruptions were directly and weakly correlated with LOS (p=0.002) and LOSNS (p=0.001). There were no significant correlations for unexpected reasons for diet interruptions.

Table 5. Correlation between nutritional support administration and clinical outcomes.

Exposures		**Clinical outcomes**	
		Length of hospital Stay (days)	Length of Hospital Stay with Nutritional Support (days)
Interval between admission and the start of nutritional support (days)	r p value (n)	**0.437** **0.001** **300**	0.020 0.732 300
Expected reasons for diet interruptions**	r p value (n)	**0.190** **0.001** **300**	**0.245** **0.001** **300**
Unexpected reasons for diet interruptions**	r p value (n)	0.023 0.692 300	0.087 0.135 300

Patients who started nutritional support within 48 hours			
Interval between admission and the start of nutritional support (days)	r p value (n)	0.005 0.972 50	0.071 0.623 50
Expected reasons for diet interruptions	r p value (n)	0.147 0.307 50	0.203 0.158 50
Unexpected reasons for diet interruptions	r p value (n)	0.050 0.730 50	0.069 0.635 50
Patients who started nutritional support in more than 48 hours			
Interval between admission and the start of nutritional support (days)	r p value (n)	**0.444** **0.001** **250**	-0.022 0.732 250
Expected reasons for diet interruptions**	r p value (n)	**0.198** **0.002** **250**	**0.246** **0.001** **250**
Unexpected reasons for diet interruptions**	r p value (n)	-0.001 0.982 250	0.090 0.157 250

*Statistically significant p-value (p<0.05). r = correlation coefficient, n = number of individuals in the analysis. Spearman Correlations.

In addition, analysis of the association between exposure variables with death and ICU admission were performed. Greater number of days between admission and the start of nutritional support (p=0.019) and greater number of unexpected reasons for diet interruptions (p=0.004) were seen among those who died during LOS. A greater number of expected reasons for interrupting the diet were observed among those with pressure ulcers (p=0.042) and risk of refeeding syndrome (p=0.005). And a shorter interval between admission and start of support was also observed in patients at risk of refeeding syndrome (p<0.001). There was no association with ICU admission. Data presented in **table 6.**

Table 6. Association between exposure variables and outcomes of death and ICU admission.

Exposure	OUTCOMES											
	Death			ICU admission			Risk of refeeding syndrome			Pressure injury		
	NO (n= 209)	YES (n= 91)	P value	NO (n= 164)	YES (n= 136)	P value	NO (n=264)	YES (n=36)	P value	NO (n=258)	YES (n=42)	P value
Interval between admission and the start of nutritional support	6.00 (3.50 - 12.00)	8.00 (4.00 - 17.00)	**0.019**	6.00 (3.00 - 13.00)	7.00 (4.00 - 13.75)	0.199	7.00 (4.00 - 14.00)	4.00 (2.00 - 5.75)	**<0.001**	6.5 (4.00 - 13.00)	6.00 (3.00 - 13.25)	0.747
Expected reasons for diet interruptions**	0.00 (0.00 - 0.06)	0.02 (0.00 - 0.07)	0.237	0.00 (0.00 - 0.06)	0.01 (0.00 - 0.06)	0.608	0.00 (0.00 - 0.05)	0.05 (0.00 - 0.10)	**0.005**	0.00 (0.00 - 0.06)	0.03 (0.00 - 0.07)	**0.042**
Unexpected reasons for diet interruptions**	0.00 (0.00 - 0.07)	0.04 (0.00 - 0.12)	**0.004**	0.00 (0.00 - 0.08)	0.03 (0.00 - 0.09)	0.069	0.02 (0.00 - 0.08)	0.00 (0.00 - 0.09)	0.846	0.02 (0.00 - 0.08)	0.04 (0.00 - 0.08)	0.192

Data presented as median and interquartile range.** median rate of events by length of hospital staying with nutritional support. Mann Whitney U Test.

Regression models for clinical outcomes according to exposure variables were performed, as shown in **Table 7**. In the linear regression, the interval between admission and the start of nutritional support as an independent variable was positively associated with LOS in all models, null and with adjustments for hospital sector, age and gender. This means that the longer the interval between admission and the start of nutritional support, the higher the LOS.

Finally, logistic regression was performed for the dependent variables of death, ICU admission, pressure injury and risk of refeeding syndrome. For admission to the ICU, the models had adjustments only for age and sex and no significant association was obtained (data not shown). However, it was noted that for death as a dependent variable, there was a positive association in all models (null and with adjustments

for sex, age and sector) with the independent variables of unexpected interruptions and interval between admission and the start of nutritional support in all the models, except the null model. It is understood that the chances of death were increased by 36x in the null model and by more than 30x in the models with adjustments for unexpected interruptions.

According to the analyses, the more expected interruptions, the greater the risk of refeeding syndrome, that is, there was a positive association for all models with adjustments. And the longer the interval between admission and initiation of nutritional support, the lower the risk of refeeding syndrome, there was an inverse association in all models. Thus, expected interruptions increased the risk of refeeding syndrome by up to 29x. And there was 14% protection from the risk of refeeding syndrome in the longer interval between admission and initiation of nutritional support.

Table 7. Regression models for clinical outcomes according to exposure variables.

Dependent variables	**Null Models**			**Adjusted Models[1]**			**Adjusted Models[2]**			**Adjusted Models[3]**		
	R^2	**β**	**p value**	**R^2**	**β**	**p value**	**R^2**	**β**	**p value**	**R^2**	**β**	**p value**
Interval between admission and the start of nutritional support (independent variable)												
Length of hospital Stay (days)	0.347	0.589	<0.001	0.351	0.582	<0.001	0.357	0.584	<0.001	0.360	0.581	<0.001
Dependent variables	**Null Models**			**Adjusted Models[1]**			**Adjusted Models[2]**			**Adjusted Models[3]**		
	OR	**95%CI**	**p value**	**OR**	**95%CI**	**p value**	**OR**	**95%CI**	**p value**	**OR**	**95%CI**	**p value**
Interval between admission and the start of nutritional support (independent variable)												
Death	1.013	(0.99 - 1.03)	0.084	1.016	(1.00 - 1.03)	0.045	1.017	(1.00 - 1.03)	0.034	1.016	(1.00 - 1.03)	0.046
Risk of refeeding syndrome	0.866	(0.793-0.947)	0.002	0.869	(0.795 - 0.950)	0.002	0.865	(0.791-0.947)	0.002	0.871	(0.798-0.951)	0.002

Expected interruptions (rate of events) (independent variable)												
Risk of refeeding syndrome	24.16	(0.99 - 591.10)	0.051	25.57	(1.08 - 603.32)	0.044	29.42	(1.18 - 735.12)	0.039	27.82	(1.07 - 722.08)	0.045
Unexpected interruptions (independent variable)												
Death	36.414	(2.94 - 451.53)	0.005	30.852	(2.4 - 396.61)	0.008	35.455	(2.58- 487.04)	0.008	25.377	(1.90 - 339.38)	0.015

Simple linear regression model and Binary logistic regression model. Null Models: each variable was inserted in the linear regression analysis without the addition of any adjustment variable. Adjusted Models[1]: adjusted for age; Adjusted Models[2]: adjusted for age and sector; Adjusted Models[3]: adjusted for age, sector and sex. R^2= R-squared. - = non-significant data.
CI, confidence interval; OR, odds ratio

Discussion

The results obtained in the present study demonstrate that most patients were already malnourished when they started the nutritional support and for most patients the start of nutritional support occurs after 48 hours of hospital admission. The introduction of the nutritional support after 48h of hospital admission was associated with higher mortality, longer LOS and inversely with risk of refeeding syndrome. Furthermore, 2/3 of patients had at least one diet infusion interruption during LOSNS and most of them are due to unexpected reasons. However, only the expected interruptions of diet infusion had a negative impact on clinical outcomes of patients. Greater LOS, LOSNS, the greater the risk of refeeding syndrome and pressure injury was associated with more expected diet interruption. Unexpected interruptions were only associated with higher mortality.

Approximately 61.9% of the patients who presented in this sample had moderate or severe malnutrition. This finding reinforces the high prevalence of hospital malnutrition, which leads to worse clinical outcomes due to impaired nutritional status during hospitalization (19, 20). This association can be explained by the association of the presence of risk factors in hospitalized patients. Hospitalization itself is a risk factor for malnutrition due to the inadequate number of offered meals, greater need for care, and also, food selectivity is common, and it promotes the decline in nutritional status (21). The review by Bellanti and colleagues (19) addresses other factors such as aging, presence of multiple comorbidities, use of medication (polypharmacy), especially proton pump inhibitors, anticonstipation and antihypertensive drugs, in addition to low functional capacity, alcohol abuse, depression, tobacco use, or socioeconomic status. In addition, the decline in nutritional status impacts loss levels and increases mortality rates with consequent high costs and risk of complications. Studies show that malnourished patients have about 40–70% higher LOS compared to healthy ones (22, 23).

However, it is well known that nutritional intervention during hospitalization can minimize the harm caused by malnutrition. ESPEN and ASPEN guidelines suggest screening for malnutrition, nutritional assessment and nutritional support for hospitalized patients with malnutrition due to positive outcomes in mortality and complications and improved functional outcomes associated with it (19). A systematic review and meta-analysis reported that nutritional support was associated with up to a 53% reduction in the risk of mortality rate (24). Pratt and colleagues (25) found a 25% reduction in length of stay (from 8 to 6 days, $p<0.01$) and a 35.7% reduction in infection rates (from 14% to 9%, $p< 0.01$) for malnourished patients after implementation of nutritional intervention. Kaegi-Braun and collaborators (26) found that nutritional support is associated with a statistically significant reduction in patient mortality

(7.2% versus 8.8%; incidence rate, 0.79 [95% CI, 0 .75-0.84]; P < 0.001). These findings are similar to what was seen with the patients studied.

It was seen that in the present study, most of the sample (83.3%) started nutritional support late. A median of 6 days between hospitalization and the start of nutritional support was observed in this sample. Guidelines suggest that nutritional support should start between 24 and 48 hours after admission (27) in cases of polymorbid patients. Especially in malnourished patients, the ideal is to start EN early because of the benefits to nutritional status, attenuation of disease severity and stress modulation (28,29). Corroborating our findings, studies show that patients who did not receive early EN had higher mortality in the ICU and hospital, in addition to a higher incidence of complications, failure to reach nutritional goals, and a higher rate of pressure injuries (30,31). Considering these data, it is noteworthy that in cases where the onset of EN is postponed, as in the present study, the chances of associated complications increase, further revealing the importance of following the recommendations of the guidelines to prevent complications and improve the clinical outcomes. Kaneko et al. (32) demonstrated that late initiation of feeding (more than 48 hours after admission) was associated with higher hospital mortality (OR 1.32, 95% CI 1.26 to 1.39) and longer LOS and higher incidence of pneumonia and sepsis when compared to earlier initiation of feeding. A study that compared early EN with late EN found a lower risk of hospital death in the first group, around 40% and 53% compared to 47% and 60% in the second (29). Early initiation also reduced mortality in critically ill patients (33) and patients with Coronavirus Disease 2019 (34). Late initiation of nutrition can also lead to higher rates of infections, worsening the clinical picture. A systematic review of 11 studies found a reduction in the risk of infection in early compared to late nutrition (RR 0.64; CI 95% 0.46–0.90; P = 0.010; I 2 = 25%) (35).

Despite these data, the timing of nutrient delivery is crucial, and in some cases, starting later can be beneficial. An example is the study by Osuna-Padilla (36) whose early start of EN was associated with gastrointestinal intolerance in 30 to 70% of UTI patients. Situations of hemodynamic instability and greater initial severity of the disease may require the start of EN after 48 hours (37). In this study, the onset of nutritional support after 48 hours impairs the risk of refeeding syndrome. One hypothesis that explains this finding comes from the fact that the patients in this study used more than one feeding route during a hospital stay. With this, it is assumed that patients who started support late were using oral nutrition before EN and PN. With that in mind, the identification of the risk of refeeding syndrome is traditionally done, and in the hospital where the study was carried out, by the marker of low serum phosphate content, which limits the diagnosis and early detection of the risk (38). The major limitation of this form of hypophosphatemia detection as an indicator of advanced confidence syndrome is the fact that phosphate determinations are not routine in clinical practice, which can lead to

underreporting of the real risk (39). In most cases, phosphorus monitoring is performed after starting nutritional support, due to the higher incidence related to EN (21.4% versus 8.5%) than to PN (38). Furthermore, the data show that not only are ¼ of critically ill patients admitted with hypophosphatemia, but this is not always identified due to a change being recorded as a phosphate level below an absolute level rather than as a percentage drop, although within the normal reference range, which can lead to confusion and make diagnosis difficult (38,40). However, it is emphasized that the prolonged postponement of EN is harmful, since nutritional support must meet the needs of patients, reducing complications and worsening of the clinical condition (28,41).

The diet infusion interruptions were frequent in this sample, especially in the ICU, and it compromises the achievement of patients' nutritional goals, increasing the risk of malnutrition (42). It is known that many of the interruptions are necessary in the clinical context, such as fasting for the performance of procedures, exams, and interruptions for routine nursing care, such as tube repositioning or medication administration (43). However, our findings reflect that even expected diet infusion interruptions should be carefully considered, as they may lead to a greater risk of refeeding syndrome, LOS and mortality. This relationship can be explained due to the profile of hospitalized patients that commonly have significant malnutrition and, therefore, a higher risk of clinical complications and greater nutritional demand (44). The routine interruptions lead to a smaller diet infusion, and it may impact on the clinical outcomes of patients (45).

Refeeding syndrome has a wide incidence in hospitalized patients, from 0.43% to 18% depending on the profile of the patient; a higher risk is seen in the elderly, critically ill patients, with cancer and adults with malabsorption (46,47). The mentioned risk groups are similar to the participants of the present study, therefore, interrupt diet offers may lead to severe clinical outcomes, even risk of death, as it was seen with the presented data. The study by Ribeiro et al. (48) showed that 78.1% of the total paused hours of diet infusion were due to interruptions for procedures such as extubating and gastrointestinal complications or routine procedures. It is noteworthy that even planned breaks can affect the achievement of nutritional needs and when this is affected, the nutritional status of patients is compromised, increasing the risk of refeeding syndrome and the severity of its manifestations (49). Thus, the implementation of institutional protocols should be encouraged to minimize the aforementioned effects.

Supplying nutritional support has its challenges, and even expected interruptions can lead to issues such as increased risk of pressure injury. This finding in the present study can be explained by the fact that nutritional deprivation and insufficient food intake are the main risk factors for the development of pressure injury. Previous studies have shown that factors such as malnutrition, undernourishment and age, especially 65 years or older, are risk factors

for the development of pressure ulcers (50,51). Adequate nutritional support plays an essential role in preventing pressure ulcers and stimulating wound healing but is often interrupted or delayed (44,52). The global prevalence of pressure injury is around 14.8% and, when diagnosed, it increases costs, reduces quality of life and increases LOS, resulting in a greater economic burden (52). As malnutrition is closely linked to pressure injuries and patients need a greater supply of nutrients due to increased energy needs, early diagnosis and prevention of exacerbation of injuries is essential. Another important measure is monitoring the provision of adequate nutrition to minimize associated costly and preventable adverse events (53).

However, several interruptions are avoidable, and sometimes it usually happens for prolonged fasting period or lack of prescription (43). In the prospective observational study by Peev and collaborators (45), the most common reasons for interruptions in EN infusion were to perform procedures, with 26% considered avoidable interruptions. The patients who had interruptions, experienced a higher caloric deficit, longer LOS, and longer ICU stays. The authors found that having at least 1 diet infusion interruption was proportional to 3 times more likely to not achieve nutritional needs (<66% of total calories prescribed) (45). Unexpected interruptions usually happen due to clinical complications, such as metabolic, mechanical and gastrointestinal complications (43). These interruptions generally aim to protect patients from worse injuries that would compromise the clinical picture. However, our findings demonstrate that those who died had a higher number of unexpected diet interruptions. This finding can be explained by the severity of the patient, since polymorbid patients have a high risk of malnutrition and, consequently, higher mortality (54).

Although this is a relevant and unique study on the subject, some limitations must be explored. First, it is an observational study using secondary data, therefore, all the information used came from the professionals' medical records. This practice can allow systematic errors to be recognized and not be clearly identified. In addition, the sample, despite being robust, is very heterogeneous. The patients had different pathologies and specific clinical conditions, which, when evaluated together, were not considered. Finally, quantifying the interruptions is a complex task, as the patient sometimes received more than one type of nutrition, and this may have generated an overestimation of values. Although the pointed limitations, measures were taken to minimize confounding factors. The entire team underwent rigorous training before data collection, missing and conflicting information was checked in the system again, and the methodology was rigorous to obtain reliable results. Also, commonly, prospective studies in the subject present only baseline diet infusion data and do not monitor the patient throughout the hospitalization, limiting the information on nutritional offer.

Conclusion

This study revealed that the late initiation of nutritional support is associated with a significantly increased risk of death and longer hospitalization, in addition, decreased the occurrence of pressure ulcers. Diet interruptions were also associated with a significantly increased risk of death and longer hospitalization on nutritional support, in addition, increased occurrence of pressure ulcers and increased risk of refeeding syndrome. The data obtained emphasize the importance of offering an adequate intake to patients using nutritional support and reinforce the need to monitor hospital malnutrition and diet infusion, in order to minimize health problems. More studies are needed to assess the relationship between support administration and outcomes in hospitalized patients using nutritional support.

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2. CONSIDERAÇÕES FINAIS

Os resultados deste trabalho revelaram que existe uma inadequação do aporte calórico e proteico e estes problemas, na prática do SN contribuem para um declínio do estado nutricional, com depleção da massa muscular e consequentemente, piores desfechos clínicos em pacientes hospitalizados. A redução da massa muscular foi associada a complicações do suporte nutricional e as interrupções na infusão da dieta foram associadas a maior mortalidade e maior tempo de internação, aumentando os custos e impactos econômicos ao setor de saúde.

Uma maior ingestão proteica esteve associada a menor depleção de massa muscular, proteção contra mortalidade e risco de encaminhamento à UTI. O início tardio do SN e as interrupções da dieta, mesmo quando programadas, também foram associadas a piores prognósticos como maior mortalidade.

A utilização de equações de predição de massa muscular, em detrimento a outros métodos, não disponíveis na prática clínica, possibilitou a mensuração da massa muscular destes pacientes. Entretanto, equações específicas para essa população que sejam validadas e mais sensíveis à massa muscular são necessárias para obter maior confiabilidade e precisão para uso na prática clínica.

Os dados obtidos enfatizam a importância de oferecer uma ingestão adequada aos pacientes em uso de SN e reforçam a necessidade de monitoramento da desnutrição hospitalar e da infusão de dieta, a fim de minimizar problemas de saúde. Este foi um estudo promissor na temática, por avaliar tanto a ingestão e adequação quanto os desfechos clínicos durante toda a internação em uso de SN. Contudo, mais estudos ainda são necessários para elucidar a relação entre a administração e os resultados clínicos em pacientes hospitalizados em uso de SN.

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8. APÊNDICES E ANEXOS

APÊNDICE A. Termo de Consentimento Livre e Esclarecido

O Sr. (a) está sendo convidado (a) como voluntário (a) a participar da pesquisa **"INDICADORES DE QUALIDADE E FATORES ASSOCIADOS A TERAPIA NUTRICIONAL ENTERAL E PARENTERAL EM UM HOSPITAL UNIVERSITÁRIO".** Pedimos a sua autorização para a coleta, o depósito, o armazenamento, a utilização e descarte das informações que serão coletadas. A utilização das informações está vinculada somente a este projeto de pesquisa ou se Sr. (a) concordar em outros futuros. Nesta pesquisa pretendemos avaliar o uso de terapia nutricional enteral e parenteral em um hospital de ensino e sua relação com características do paciente, da doença e complicações associadas. Para esta pesquisa adotaremos os seguintes procedimentos: os dados serão levantados diretamente com o paciente ou responsável, e na consulta ao seu prontuário, sendo que serão registrados em um formulário próprio o qual ficará na posse dos pesquisadores, que farão seu descarte após a finalização do estudo. Os riscos envolvidos na pesquisa consistem em gerar desconforto ao responder as informações, sendo que será tomado o cuidado de se manter a privacidade durante a coleta. A pesquisa contribuirá para avançar na qualidade assistencial aos pacientes em uso de terapia nutricional.

Para participar deste estudo o Sr. (a) não terá nenhum custo), nem receberá qualquer vantagem financeira. Apesar disso, caso sejam identificados e comprovados danos provenientes desta pesquisa, o Sr.(a) tem assegurado o direito à indenização. O Sr. (a) terá o esclarecimento sobre o estudo em qualquer aspecto que desejar e estará livre para participar ou recusar-se a participar e a qualquer tempo e sem quaisquer prejuízos, pode retirar o consentimento de guarda e utilização das informações levantadas, valendo a desistência a partir da data de formalização desta.

A sua participação é voluntária, e a recusa em participar não acarretará qualquer penalidade ou modificação na forma em que o Sr. (a) é atendido (a) pelo pesquisador, que tratará a sua identidade com padrões profissionais de sigilo. Os resultados obtidos pela pesquisa, estarão à sua disposição quando finalizada. Seu nome será mantido em sigilo. O (A) Sr. (a) não será identificado (a) em nenhuma publicação que possa resultar.

Este termo de consentimento encontra-se impresso em duas vias originais, sendo que uma será arquivada pelo pesquisador responsável, na Escola de Enfermagem da UFMG, sala 202, e a outra será fornecida ao Sr. (a). Os dados, materiais e instrumentos utilizados na pesquisa ficarão arquivados com o pesquisador responsável por um período de 5 (cinco) e após esse tempo serão destruídos. Os pesquisadores tratarão a sua identidade com padrões profissionais de sigilo, atendendo a legislação brasileira (Resoluções Nº 466/12; 441/11 e a Portaria 2.201 do Conselho Nacional de Saúde e suas complementares), utilizando as informações somente para fins acadêmicos e científicos.

Eu, _____, portador do documento de Identidade _____ fui informado (a) dos objetivos, métodos, riscos e benefícios da pesquisa **"INDICADORES DE QUALIDADE E FATORES ASSOCIADOS A TERAPIA NUTRICIONAL ENTERAL E PARENTERAL EM UM HOSPITAL UNIVERSITÁRIO"** , de maneira clara e detalhada e esclareci minhas dúvidas. Sei que a qualquer momento poderei solicitar novas informações e modificar minha decisão de participar se assim o desejar.

Rubrica do pesquisador: _____

*Rubrica do participante:*_____

( ) Concordo que as informações coletadas sejam utilizadas somente para esta pesquisa.

Declaro que concordo em participar desta pesquisa. Recebi uma via original deste termo de consentimento livre e esclarecido assinado por mim e pelo pesquisador, que me deu a oportunidade de ler e esclarecer todas as minhas dúvidas.

_____

Nome completo do participante Data

_____

Assinatura do participante

Nome completo do Pesquisador Responsável: Camila Kümmel Duarte e Jaqueline A. Guimarães Barbosa
Endereço: Av. Alfredo Balena, 190. CEP: 30130100 / Belo Horizonte – MG
Telefones: (31) 3409-9857
E-mail: jaqueline@task.com.br; camila.kummel@gmail.com;

_____

Assinatura dos pesquisadores responsáveis
Data

Em caso de dúvidas, com respeito aos aspectos éticos desta pesquisa, você poderá consultar:
COEP-UFMG - Comissão de Ética em Pesquisa da UFMG
Av. Antônio Carlos, 6627. Unidade Administrativa II - 2º andar - Sala 2005.
Campus Pampulha. Belo Horizonte, MG – Brasil. CEP: 31270-901.
E-mail: coep@prpq.ufmg.br. Tel: 34094592.

Rubrica do pesquisador: _____
*Rubrica do participante:*_____

APÊNDICE B. Ficha de Coleta

Nome:	Data de Nascimento:	Registro:	TCLE: ()Assinado ( ) Pendente	
Leito:	Sexo: ( )F ( ) M	Idade:	Raça/cor:	Município:
Internação no HC:	Setor da internação:	Tempo de internação prévia (Local e data):		
Diagnóstico Médico:				
História Médica Pregressa:				
Histórico da Internação antes do Suporte:				
Tratamento cirúrgico:				
Tratamento farmacológico:				
Situação: Alta: __/__/__ Óbito ( ) sim ( ) não Se sim, data:__/__/__				

Data Dia: / /			Dia:__/__/__	Dia:__/__/__	Dia:__/__/__	Dia:__/__/__	Dia:__/__/__	Dia:__/__/__	Dia:__/__/__	Dia:__/__/__
Prescrições	Terapia Nutricional		() VO () NE () NPT	() VO () NE () NPT	() VO () NE () NPT	() VO () NE () NPT	() VO () NE () NPT	() VO () NE () NPT	() VO () NE () NPT	() VO () NE () NPT
	NE	Via de acesso	() CNE () CNG () GTT () JJT () COE () CNO () NA	() CNE () CNG () GTT () JJT () COE () CNO () NA	() CNE () CNG () GTT () JJT () COE () CNO () NA	() CNE () CNG () GTT () JJT () COE () CNO () NA	() CNE () CNG () GTT () JJT () COE () CNO () NA	() CNE () CNG () GTT () JJT () COE () CNO () NA	() CNE () CNG () GTT () JJT () COE () CNO () NA	() CNE () CNG () GTT () JJT () COE () CNO () NA
	NE	Fórmula	() PADRÃO () HIPERPROT. () HIPERCAL. () NI () NA	() PADRÃO () HIPERPROT. () HIPERCAL. () NI () NA	() PADRÃO () HIPERPROT. () HIPERCAL. () NI () NA	() PADRÃO () HIPERPROT. () HIPERCAL. () NI () NA	() PADRÃO () HIPERPROT. () HIPERCAL. () NI () NA	() PADRÃO () HIPERPROT. () HIPERCAL. () NI () NA	() PADRÃO () HIPERPROT. () HIPERCAL. () NI () NA	() PADRÃO () HIPERPROT. () HIPERCAL. () NI () NA
	NE	Volume (ml/h)								
	NE	Ad. Cal. (Kcal)								
	NE	Ad. Cal. (%)								
	NE	Ad. PTN (gr)								
	NE	Ad. PTN (%)								
	NE	Recebendo dieta	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	NE	Tipo de infusão	INTERMIT. CONTÍNUA CÍCL. NOTUR.	INTERMIT. CONTÍNUA CÍCL. NOTUR.	INTERMIT. CONTÍNUA CÍCL. NOTUR.	INTERMIT. CONTÍNUA CÍCL. NOTUR.	INTERMIT. CONTÍNUA CÍCL. NOTUR.	INTERMIT. CONTÍNUA CÍCL. NOTUR.	INTERMIT. CONTÍNUA CÍCL. NOTUR.	INTERMIT. CONTÍNUA CÍCL. NOTUR.
	NE	Tipo de catéter								
	NP	Via de acesso	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA
	NP	Fórmula								
	NP	Volume (ml/h)								
	NP	Ad. Cal. (Kcal)								
	NP	Ad. Cal. (%)								
	NP	Ad. PTN (gr)								
	NP	Ad. PTN (%)								
	NP	Recebendo dieta	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	NP	Tipo de infusão	INTERMIT. CONTÍNUA CÍCL. NOTUR	INTERMIT. CONTÍNUA CÍCL. NOTUR	INTERMIT. CONTÍNUA CÍCL. NOTUR	INTERMIT. CONTÍNUA CÍCL. NOTUR	INTERMIT. CONTÍNUA CÍCL. NOTUR	INTERMIT. CONTÍNUA CÍCL. NOTUR	INTERMIT. CONTÍNUA CÍCL. NOTUR	INTERMIT. CONTÍNUA CÍCL. NOTUR
	NP	Tipo de catéter	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA	CENTRAL PERIFÉRICA
	Ad. (Kcal)	TOTAL								
	Ad. Cal. (%)	TOTAL								
	Ad. PTN (gr)	TOTAL								
	Ad. PTN (%)	TOTAL								

Avaliação	Peso (Kg) ( )A ( ) E ( ) I								
	Altura (m) ( )A ( ) E ( ) I								
	AJ (cm) ( )D ( ) E								
	CP (cm) ( )D ( ) E								
	CB (cm) ( )D ( ) E								
	FPM ( )D ( ) E								
	IMC (kg/m²)								
	Edema	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Local do edema	MMII MMSS ANA	MMII MMSS ANA	MMII MMSS ANA	MMII MMSS ANA	MMII MMSS ANA	MMII MMSS ANA	MMII MMSS ANA	MMII MMSS ANA
Nutricional	Diagnóstico Nutricional								
Exames	Fósforo (P)								
	Potássio (K)								
	Magnésio (Mg)								
	Sódio (Na)								
	PCR								
	Albumina (Alb)								
	Creatinina (Cr)								
	Creatina Kinase (CK)								
	Exames adicionais:								
Complicações	Interrupção da dieta	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Motivos								
	Febre	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Aspiração	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Obstrução Sonda	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Constipação	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Colestase	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Colelitíase	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Diarreia	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO

	Distensão Abdominal	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Ascite	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Esteatose	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Exteriorização Sonda	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Gastroparesia	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Hiperglicemia	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Hipoglicemia	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Hipertrigliceridemia	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Hipercalemia	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Hiperfosfatemia	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Hipernatremia	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Infecção Cateter	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Lesão por Pressão	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Local LPP								
	Náuseas	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Vômitos	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Estase	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Volume da Estase								
	Diálise (TRS)	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Pneumotórax	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	SRA	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
Observações:									

Desfechos	Cuidados Paliativos	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Data de internação no CTI - Data de saída do CTI								
	Alta para Via Oral	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Alta da Nutrição								
	Alta Hospitalar	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Alta Hospitalar com Suporte	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Reinternação no Suporte Nutricional	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO
	Obito	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO	SIM NÃO

Internação total (dias):

APÊNDICE C. TERMO DE RESPONSABILIDADE DA GERÊNCIA DE ENSINO E PESQUISA DO HOSPITAL DAS CLÍNICAS DA UFMG

Universidade Federal de Minas Gerais
Hospital das Clínicas

EBSERH HOSPITAIS UNIVERSITÁRIOS FEDERAIS

TERMO DE RESPONSABILIDADE: ACESSO À DADOS CLÍNICOS EM FORMATO ELETRÔNICO PARA FINS DE PESQUISA

Política de Segurança em Tecnologia da Informação na Saúde

(Perfil de Acesso: Pesquisador)

Nome do projeto de pesquisa:

AVALIAÇÃO DA TERAPIA NUTRICIONAL ENTERAL E PARENTERAL EM UM HOSPITAL UNIVERSITÁRIO DE BELO HORIZONTE

Nome do coordenador do projeto de pesquisa e vínculo institucional:

CAMILA KÜMMEL DUARTE - PROFESSORA DO DEPARTAMENTO DE NUTRIÇÃO NA ESCOLA DE ENFERMAGEM DA UNIVERSIDADE FEDERAL DE MINAS GERAIS.

Registro na Plataforma Brasil: C.A.A.E

27966620.4.0000.5149

Duração da pesquisa data de início: 13/05/2022 data de término: 20/12/ ~~2026~~ 2024

Modalidade de acesso aos dados clínicos:

( ) Consulta-prontuário dentro dos Sistemas de PEP do Hospital das Clínicas da UFMG

(X) Consulta-prontuário dentro dos Sistemas de PEP do Hospital das Clínicas da UFMG e adicionalmente registros de papel no arquivo SAME

( ) Base de dados clínica, anonimizada. Neste caso identificar o nome do sistema e o período de coleta de dados constantes no projeto autorizado pelo CEP UFMG

( ) Base de dados clínica identificada. Neste caso identificar o nome do sistema e o período de coleta de dados constantes no projeto autorizado pelo CEP UFMG

( ) Outra modalidade (especificar):

Identificação da equipe de pesquisa que terá acesso aos sistemas eletrônicos, quando for o caso:

Pesquisador 1 (nome e vínculo): Luciana de Abreu Silva (aluna de pós-graduação UFMG)
Pesquisador 2 (nome e vínculo): Maria Izabel Fortes (aluna de graduação UFMG)

Av. Prof. Alfredo Balena, 110 – 1º andar
Bairro Santa Efigênia – Cep: 30130-100 – Belo Horizonte – MG
Telefone: (31) 3409.9612 - FAX: (31) 3409.9380 –
E-mail: dirgerai@hc.ufmg.br

Universidade Federal de Minas Gerais
Hospital das Clínicas

EBSERH
HOSPITAIS UNIVERSITÁRIOS FEDERAIS

Eu, Camila Kümmel Duarte, SIAPE: 3.029.908, CPF: 017.027.450.07, declaro ter conhecimento de que as informações constantes no prontuário clínico pertencem ao paciente, estão sob a guarda do Hospital das Clínicas da Universidade Federal de Minas Gerais, administrado pela Empresa Brasileira de Serviços Hospitalares, e são de caráter sigiloso. Eu concordo em tomar todas as precauções para assegurar a Confidencialidade, Integridade e Disponibilidade de qualquer informação, seja ela interna ou externa, que tenha sido confiada a mim pela no exercício de minha atuação como pesquisador.

Assumo o compromisso de utilizar os dados apenas para os fins previstos no projeto de pesquisa supracitado, já aprovado pelo CEP UFMG e pela Gerência de Ensino e Pesquisa do Hospital das Clínica da UFMG. Assumo o compromissode não repassar os dados para quaisquer outros que não os membros da equipe de pesquisa sob minha coordenação. Estou ciente de que o acesso, a cópia ou a divulgação indevida dos dados constantes no prontuário do paciente constitui infração grave ou crime, em conformidade com a resolução CFM nº 1605/2000 (do Conselho Federal de Medicina); artigo 154 do Código Penal; artigos 73, 74, 75, 76, 77, 78, 79 e 85 do Código de Ética Médica; artigo 5º, inciso X, da Constituição Federal.

Estou ciente de que embora a lei n.º 12.527/11, - Lei de Acesso à Informação, tenha sido criada com a finalidade de garantir o acesso às informações, em seu capítulo IV seção V, restringe o acesso às informações sigilosas, somente às pessoas que necessitem conhecê-las como médicos, profissionais e estudantes da área da saúde, e delega a quemas usou, a obrigação do sigilo e a responsabilidade por seu uso indevido.

Belo Horizonte, 13 de Maio de 2022.

Camila K Duarte

Assinatura e carimbo profissional (Pesquisador Responsável)

Observações e especificidades do projeto de pesquisa se for o caso):

Ciência da Gerência de Ensino e Pesquisa

Belo Horizonte, 13 de Maio de 2022.

Profª Tiana Maria Kakehasi
Gerente de Ensino e Pesquisa
Insc. 219738 C.A 30769
PT - SEI 342 de 20/05/19
HC-UFMG/EBSERH

Assinatura do Gerente de Ensino e Pesquisa

Av. Prof. Alfredo Balena, 110 – 1º andar
Bairro Santa Efigênia – Cep: 30130-100 – Belo Horizonte – MG
Telefone: (31) 3409.9612 - FAX: (31) 3409.9380 –
E-mail: dirgeral@hc.ufmg.br

ANEXO 01. PARECER DA COMISSÃO DE ÉTICA EM PESQUISA DA UFMG

UNIVERSIDADE FEDERAL DE MINAS GERAIS

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: AVALIAÇÃO DA TERAPIA NUTRICIONAL ENTERAL E PARENTERAL EM UM HOSPITAL UNIVERSITÁRIO DE BELO HORIZONTE

Pesquisador: Camila Kümmel Duarte

Área Temática:

Versão: 1

CAAE: 27966620.4.0000.5149

Instituição Proponente: Escola de Enfermagem

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 3.964.351

Apresentação do Projeto:

A Terapia Nutricional (TN) é um conjunto de procedimentos que visa manter ou recuperar o estado nutricional do paciente, por meio de suplementação da via oral (SVO), Nutrição Enteral (NE) e/ou Parenteral (NP), garantindo o aporte adequado de nutrientes. Contudo, como toda terapêutica, a TN também não é isenta de riscos e complicações. Desta forma, este trabalho tem como objetivo avaliar a prática da terapia nutricional enteral e parenteral em um hospital público de ensino. Trata-se de estudo observacional prospectivo a ser realizado em um único hospital público de ensino. Todos os dados serão coletados por estudantes treinados e por profissionais do serviço, sob supervisão dos pesquisadores responsáveis. A equipe da Comissão de Suporte Nutricional do HC da UFMG repassará aos pesquisadores a identificação dos pacientes admitidos na equipe de suporte nutricional do HC. Os pesquisadores entrarão em contato com o paciente e/ou acompanhante para assinatura do termo de consentimento livre e esclarecido (TCLE). Após a assinatura do TCLE, os pesquisadores iniciarão a coleta de dados das fichas clínicas e prontuário eletrônico. Nenhum dado será solicitado diretamente ao paciente, seu acompanhante ou para os profissionais que o acompanham. Após o preenchimento de fichas, os dados serão computados em banco de dados eletrônicos. A amostra deste estudo será composta por todos os pacientes maiores de 18 anos que iniciarem TN enteral ou parenteral no Hospital das Clínicas da UFMG e estiverem sob acompanhamento da Comissão de Terapia Nutricional do HC da UFMG. Os dados coletados serão digitados em uma planilha de Excel® e posteriormente serão transportados para o

Endereço: Av. Presidente Antônio Carlos,6627 2º Ad SI 2005
Bairro: Unidade Administrativa II **CEP:** 31.270-901
UF: MG **Município:** BELO HORIZONTE
Telefone: (31)3409-4592 **E-mail:** coep@prpq.ufmg.br

software estatístico SPSS® para análises. Para a comparação das características clínicas e laboratoriais dos pacientes será usada o teste t de Student ou teste de Mann-Whitney para amostras independentes conforme a distribuição dos dados. Para as variáveis categóricas serão utilizados o Teste Exato de Fisher ou Qui-quadrado. Serão analisados também os coeficientes de correlação de Pearson ou Spearman, conforme indicado. Para avaliar a associação entre as características da TN ou dos pacientes com o surgimento de complicações da TN ou desfechos clínicos será usada análise de regressão linear ou logística, conforme características das variáveis dependentes.Os dados serão expressos como média ± desvio padrão ou como mediana e variação no caso de dados de distribuição não normal. O nível de significância adotado será de 5%.

Objetivo da Pesquisa:

De acordo com os proponentes, o objetivo primário do projeto é "avaliar a prática da terapia nutricional enteral e parenteral em um hospital público de ensino."

Como objetivos secundários pretende-se:

• Caracterizar o perfil sócio-demográfico e clínico dos pacientes em uso de TNE e/ou TNP na Instituição; • Identificar os cateteres utilizados para a infusão da TNE e TNP e as complicações relacionadas; • Avaliar a infusão das dietas e o alcance das metas calóricas e proteicas; • Avaliar as complicações clínicas dos pacientes em uso da TNE e TNP; • Avaliar desfechos clínicos dos pacientes em uso da TNE e TNP. • Avaliar a qualidade da TNE e TNP.

Avaliação dos Riscos e Benefícios:

Os possíveis riscos da pesquisa são a divulgação de dados confidenciais, invasão de privacidade, interferência na rotina dos atendimentos, riscos físicos (relativos à antropometria), riscos à segurança dos prontuários. Contudo, os profissionais serão capacitados para evitarem e/ou minimizarem ao máximo esses riscos, atentando para sinais verbais e não verbais manifestados pelos participantes. Serão coletadas apenas informações necessárias ao desenvolvimento da pesquisa. Serão tomados todos os cuidados para assegurar a privacidade e sigilo dos dados. Será assegurada a inexistência de conflito de interesse. Benefícios: Com o estudo espera-se contribuir com melhorias no uso da terapia nutricional enteral e parenteral em hospitais, através da identificação de fatores associados ao prognóstico do paciente e otimização da oferta da TN. Os resultados serão divulgados em ambas instituições envolvidas, e em eventos científicos nacionais e internacionais, conforme oportunidades, bem como em periódicos científicos a fim de contribuir para avanços no conhecimento da área.

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Continuação do Parecer: 3.964.351

Comentários e Considerações sobre a Pesquisa:

Pesquisa relevante para a área.

Considerações sobre os Termos de apresentação obrigatória:

Foram apresentados os seguintes documentos: folha de rosto assinada; projeto completo; parecer com aprovação da Câmara Departamental; TCLE; Formulário de Informações Básicas; TCUD.

Recomendações:

Não há.

Conclusões ou Pendências e Lista de Inadequações:

O projeto poderá ser aprovado, SMJ.

Considerações Finais a critério do CEP:

Tendo em vista a legislação vigente (Resolução CNS 466/12), o CEP-UFMG recomenda aos Pesquisadores: comunicar toda e qualquer alteração do projeto e do termo de consentimento via emenda na Plataforma Brasil, informar imediatamente qualquer evento adverso ocorrido durante o desenvolvimento da pesquisa (via documental encaminhada em papel), apresentar na forma de notificação relatórios parciais do andamento do mesmo a cada 06 (seis) meses e ao término da pesquisa encaminhar a este Comitê um sumário dos resultados do projeto (relatório final).

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1489506.pdf	06/01/2020 14:58:35		Aceito
Declaração de Instituição e Infraestrutura	Parecer.pdf	13/12/2019 17:38:53	Camila Kümmel Duarte	Aceito
Projeto Detalhado / Brochura Investigador	ProjetoFinal.docx	13/12/2019 17:38:26	Camila Kümmel Duarte	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCUD.docx	13/12/2019 17:37:36	Camila Kümmel Duarte	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.docx	13/12/2019 17:37:17	Camila Kümmel Duarte	Aceito
Folha de Rosto	folha.pdf	13/12/2019	Camila Kümmel	Aceito

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Continuação do Parecer: 3.964.351

Folha de Rosto	folha.pdf	17:37:05	Duarte	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

BELO HORIZONTE, 10 de Abril de 2020

Assinado por:
Críssia Carem Paiva Fontainha
(Coordenador(a))

Endereço: Av. Presidente Antônio Carlos,6627 2º Ad SI 2005
Bairro: Unidade Administrativa II **CEP:** 31.270-901
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ANEXO A. Comprovante de submissão do Artigo 1

- Journal of Parenteral and Enteral Nutrition

Gmail — Luciana Abreu <lucianabreu.silva@gmail.com>

Journal of Parenteral and Enteral Nutrition Manuscript ID - JPEN-2023-02-059
2 mensagens

Sarah Wolper <onbehalfof@manuscriptcentral.com> 27 de fevereiro de 2023 às 12:02
Responder a: jpen@nutritioncare.org
Para: lucianabreu.silva@gmail.com
Cc: lucianabreu.silva@gmail.com, simonenutufmg@gmail.com, vanessa.moreira@ebserh.gov.br, lincolnantinossi@yahoo.com.br, carolfcast@gmail.com, nanavassallo@gmail.com, brunaguerrac@gmail.com, camila.kummel@gmail.com

27-Feb-2023

Dear Miss Silva:

Your manuscript entitled "Muscle mass, nutritional intake and clinical outcomes of patients using nutritional support: a prospective cohort study" has been successfully submitted online and is presently being given full consideration for publication in the Journal of Parenteral and Enteral Nutrition.

Your manuscript ID is JPEN-2023-02-059.

Please mention the above manuscript ID in all future correspondence or when calling the office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at https://mc.manuscriptcentral.com/jpen and edit your user information as appropriate.

Our journal is currently transitioning to Wiley's Research Exchange submission portal. If you submitted this manuscript through our Research Exchange site, you can view the status of your manuscript by logging into the submission site at wiley.atyponrex.com/journal/JPEN.

If you submitted this manuscript through ScholarOne, you can view the status of your manuscript by checking your Author Center after logging in to https://mc.manuscriptcentral.com/jpen .

Thank you for submitting your manuscript to the Journal of Parenteral and Enteral Nutrition.

Sincerely,
Journal of Parenteral and Enteral Nutrition Editorial Office

ANEXO B. Parecer dos revisores - Artigo 1

- Journal of Parenteral and Enteral Nutrition

Gmail — Luciana Abreu <lucianabreu.silva@gmail.com>

Decision on Manuscript ID JPEN-2023-02-059
3 mensagens

Sarah Wolper <onbehalfof@manuscriptcentral.com> 15 de maio de 2023 às 15:02
Responder a: jpen@nutritioncare.org
Para: lucianabreu.silva@gmail.com
Cc: kbchristopher@bwh.harvard.edu

15-May-2023

Dear Miss Silva:

Following a thorough peer review, your manuscript JPEN-2023-02-059 entitled "Muscle mass, nutritional intake and clinical outcomes of patients using nutritional support: a prospective cohort study" which you submitted to the Journal of Parenteral and Enteral Nutrition is being returned to you for revision. The comments of the reviewer(s) are available for your guidance in preparing the revision.

Editor in Chief, Journal of Parenteral and Enteral Nutrition
kbchristopher@bwh.harvard.edu

Editor's Comments to Author:

Editor in Chief: Christopher, Kenneth
Comments to Author: Thank you for the opportunity to review your work. There are several opportunities for clarity that will improve the manuscript. Please address all of the following.
The study is defined as a prospective cohort study in the title but does not test a hypothesis. The methods indicate that "The significance level adopted for rejecting the null hypothesis was..." but do not state the study hypothesis or the alternate hypothesis that is being tested.

The study presents several exposure outcome relationships so appears to be a descriptive cohort study rather than an analytical cohort study (e.g., prospective cohort study). Descriptive cohort studies are hypothesis generating, analytical cohort studies are designed to test specific hypothesis. JPEN prefers to publish analytical studies but does publish high quality descriptive cohort studies.

An analytical cohort study is designed to determine the association between a single exposure of interest and a single primary outcome. If your study is analytic cohort study then please attend to the following:

Please state your exposure: Our exposure of interest was... defined by ...
Please state your primary outcome: Our primary outcome was...defined by... Our secondary outcomes were...
Please state your testable hypothesis as it relates to your exposure of interest and primary outcome.
Please center your results on the adjusted association between the exposure of interest and the primary outcome noted in the hypothesis.
The title needs to reflect the exposure of interest-primary outcome association under study and include the study design as a subtitle (e.g. Association between exposure and outcome in population: A retrospective cohort study")
Please minimize abbreviations or acronyms as it makes for a difficult read. Please spell out MM as muscle mass throughout the paper.

Minor issues:
Please change the following
All data were arranged in an Excel® spreadsheet database and subsequently transferred to the statistical software Statistical Package for Social Sciences (SPSS®) version 20.0 (Chicago, IL, USA). The significance level adopted for rejecting the null hypothesis was p< 0.05 and confidence interval of 95%.

Reviewer(s)' Comments to Author:

Reviewer: 1

Comments to the Author
Dear authors, thank you for the opportunity to review your manuscript. In this paper the authors report a prospective cohort of patients admitted to a nutritional support program and aim to assess the variation in muscle mass (estimated by anthropometric equations) and its relationship with nutritional intake and clinical outcomes. The main results of this study were: 1) there is a reduction in muscle mass during hospitalization; 2) higher protein intake was correlated with higher lean soft tissue; 3) patients that had more complications were more prone to lose muscle mass. Although the study question is very interesting and relevant, there are several limitations in its design and reporting. Below there are some suggestions to the authors.

Major issues

1) The association between nutritional intake and muscle mass variation in highly biased as patients with higher disease severity in general receive less calories and proteins (because of clinical instability, shock, need for procedures or intolerance) and are more prone to lose muscle mass (higher severity of disease is usually accompanied by a catabolic state). The authors should give more data regarding disease severity, especially when comparing patients with and without muscle mass loss. Without that information, is not possible to infer if change in muscle mass was secondary to nutritional support or to other confounders.

2) Muscle mass was compared at admission and discharge from the nutritional program. However, the time spent in the nutritional program was different between patients. Patients with different lengths of stay may have different exposures to nutritional support with different muscle mass trajectories. For example, a patient who received 6 days of nutritional support is likely to have a different muscle mass variation than a patient treated for 2 months. This makes the study population very heterogeneous and makes it difficult to interpret the results. An analysis of muscle mass variation over time (similar to a survival analysis) would be more informative.

3) Considering the study outcomes, death is a competing risk, as patients that died can't be further exposed to nutritional support and variate their muscle mass. This may bias the results in both directions: patients who died early may not have time enough to lose muscle mass (smoothing the loss of muscle mass); or they may not have time to recover muscle mass (as is expected to occur in some survivors), increasing muscle mass variation. Authors should consider the impact of death as competing risk in this study, which may be assessed on a sensitivity analysis or by including a competing risk model.

4) Authors should be cautious in concluding that higher nutritional intake improves outcomes. This is an observational study, therefore only associations can be observed, as the lack of control for confounding variables makes it difficult to define causality. That said, I suggest the authors in page 16, line 31, modify "greater protein intake seems to prevent MM depletion", to "greater protein intake was associated to less MM depletion" and remove the last phrase of conclusion.

5) The abstract conclusion does not answer the study question. I suggest the authors modify it.

6) I could not understand the proposed sample size calculation. This was an observational study, with the aim of evaluating the variation in muscle mass over time and its relationship with nutritional intake. The authors did not intend to demonstrate differences in length of stay (or at least that was not the main objective of the study). Furthermore, considering the nature of the study, I believe that sample size calculation is not necessary. I suggest that the authors remove it.

7) During the analysis the authors did more than a hundred comparisons between groups, which results in a high risk for type 1 error. This should be addressed as a limitation of this study.

8) Caloric and protein balance was estimated based on total received and total prescribed. However, the amount of nutritional support prescribed does not necessarily fits the energy expenditure and nitrogen balance, which may be higher or lower. In fact, the authors measured adequacy to nutritional prescription. I suggest that the authors modify the text to address this issue.

Minor issues

1) I suggest the authors review the English wording of the manuscript. In general, the text is well written, however some phrases are literal translations from Portuguese that may be misinterpreted by native English speakers. Assistance from an English language specialist can help improve your manuscript's grammar and style.

2) References in the text must be identified with Arabic numerals, following the journal's recommendations.

3) The authors report on page 7, line 44, that 11 equations were included in the study, but only 7 equations were presented in table S1 and 3 of them are variations for women. I suggest that the authors clarify this issue.

4) If possible, it would be interesting to have more details regarding nutritional support (percent of enteral or parenteral feeding), admission diagnosis and about complications (percent of each complication).

5) As an mono-centric study, is important for readers to have more details about the Hospital where the study was conducted (e.g. number of beds, hospitalizations per year, type of admissions – surgical, medical, trauma…).

6) The method of recruitment is not clear (all patients sequentially admitted in study period? Not all patients in the hospital received a nutritional evaluation?).

7) The term “length of stay in support” is not clear (mechanical ventilation? Vasoactive drugs? Nutritional support?)

8) The authors should include the meaning of “SCre” in the text (page 8, line 31).

9) There are formatting changes throughout the text (single spacing to double spacing). Please review the text formatting following the journal's recommendations.

10) I suggest the authors include a flow chart describing screening, inclusion, and exclusion in the study (in the main manuscript or in the supplemental material).

11) Finally, I suggest that authors revise the manuscript in order to make it more objective and concise. Especially, the results and discussion chapters are long and sometimes verbose. More concise language can capture more readers' attention and convey the author's message more effectively.

Reviewer: 2

Comments to the Author
Page numbers may be a bit confusing: for example, what I label as page 4 might be page 5 as you are looking at it.

It is difficult to track the references since you have not used the traditional JPEN format of numbering them in the

body of the text.

Page 4, paragraph 3, sentence 1 - not sure what you mean by "assertive" tools

Page 4, paragraph 3, sentence 6 - were the predictive equations that you used in this study validated in hospital populations or not? Here you imply they were, but in the Conclusion of the Abstract you seem to imply that they are not.

Page 6, Clinical data, paragraph 1, sentence 1 - just a note that serum creatine is not a typical lab obtained in the clinical setting in the U.S.

Page 6, Clinical data, paragraph 2, sentence 1 - for kalemia, phosphatemia, and natremia, indicate whether you are referring to hyper or hypo conditions or both.

Page 6, Clinical data, paragraph 2, sentence 1 - place a comma between "volume" and "steatosis"

Page 6, Nutritional data, paragraph 2, sentence 1 - unclear what "on hospital admission to nutritional support" means. Do you mean when nutritional support was initiated after hospital admission?

Page 7, Nutritional data, paragraph 1, sentence 1 on this page - I am more familiar with MAC as an abbreviation for mid-arm circumference rather that median arm circumference.

Page 7, Nutritional data, paragraph 1, sentence 1- the term "a nutritional diagnostic" is vague - consider clarifying.

Page 7, Nutritional data, paragraph 1, sentence 2 - should this read "...register of the ideal body weight..."?

Page 7, Muscle mass estimation equations, paragraph 2, sentence 2 - I think it would be clarifying if you, perhaps in the Introduction or Conclusion, gave some description of the distinctions in definitions of Lean Soft Tissue, Fat-free Mass, Appendicular Lean Mass, and Skeletal Muscle Mass.

Page 9, Statistical Analysis, first paragraph on this page, sentences 6 and 7 - "eutrophic" is not a word commonly used in the U.S.

Page 15, Discussion, 2nd paragraph on this page, sentence 10 - not sure what "evitable" means.

Page 16, Discussion, 1st paragraph on this page, sentence 4 - "evolution" does not seem like the correct word here.

ANEXO C. Comprovante de submissão do Artigo 2

Fwd: Confirming submission to Clinical Nutrition
1 mensagem

Camila Kümmel Duarte <camila.kummel@gmail.com> 18 de setembro de 2023 às 13:41
Para: Luciana Abreu <lucianabreu.silva@gmail.com>

---------- Forwarded message ---------
De: **"Clinical Nutrition"** <em@editorialmanager.com>
Date: seg., 18 de set. de 2023 às 13:40
Subject: Confirming submission to Clinical Nutrition
To: Camila Kümmel Duarte <camila.kummel@gmail.com>

This is an automated message.

Association of adequacy and intake of calories and protein with clinical outcomes of patients using nutritional support: prospective study

Dear Ms. Duarte,

We have received the above referenced manuscript you submitted to Clinical Nutrition.

To track the status of your manuscript, please log in as an author at https://www.editorialmanager.com/yclnu/, and navigate to the "Submissions Being Processed" folder.

Thank you for submitting your work to this journal.

Kind regards,
Clinical Nutrition

More information and support

You will find information relevant for you as an author on Elsevier's Author Hub: https://www.elsevier.com/authors