UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS MÉDICAS: ENDOCRINOLOGIA, NUTRIÇÃO E METABOLISMO

DISSERTAÇÃO DE MESTRADO

ESTADO NUTRICIONAL E ANTROPOMÉTRICO DE PACIENTES HOSPITALIZADOS COM SÍNDROME DE IMUNODEFICIÊNCIA ADQUIRIDA (AIDS): UM ESTUDO DE COORTE PROSPECTIVO

Raissa Gorczevski

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Dissertação de Mestrado apresentada ao Programa de Pós-Graduação em Ciências Médicas: Endocrinologia da Universidade Federal do Rio Grande do Sul (UFRGS) como requisito parcial para obtenção do título de Mestre em Endocrinologia.

Orientadora: Profa. Dra. Luciana Vercoza Viana
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Porto Alegre, 2021

CIP - Catalogação na Publicação

Gorczevski, Raissa
ESTADO NUTRICIONAL E ANTROPOMÉTRICO DE PACIENTES HOSPITALIZADOS COM SÍNDROME DE IMUNODEFICIÊNCIA ADQUIRIDA (AIDS): UM ESTUDO DE COORTE PROSPECTIVO / Raissa Gorczevski. -- 2021.
39 f.
Orientadora: Luciana Vercoza Viana.

Coorientadora: Maria Helena da Silva Pitombeira Rigatto.

Dissertação (Mestrado) -- Universidade Federal do Rio Grande do Sul, Faculdade de Medicina, Programa de Pós-Graduação em Ciências Médicas: Endocrinologia, Porto Alegre, BR-RS, 2021.

1. Estado Nutricional PVHIV. 2. Síndrome da Imunodeficiência Adquirida . 3. Avaliação Antropométrica PVHIV Hospitalizados. I. Vercoza Viana, Luciana, orient. II. da Silva Pitombeira Rigatto, Maria Helena, coorient. III. Título.

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

APRESENTAÇÃO

Essa Dissertação de Mestrado segue o formato proposto pelo Programa de Pós-Graduação em Ciências Médicas: Endocrinologia, Nutrição e Metabolismo. Serão apresentados dois capítulos, sendo o primeiro composto por uma introdução sobre tema em questão e o segundo é apresentado como manuscrito com dados originais, e descreve o trabalho de pesquisa propriamente dito. A formatação dos capítulos é justificada pela escolha de envio para revista científica do segundo texto, sendo elaborado conforme normas desta publicação.

Revista para submissão do artigo original: Clinical Nutrition. (Fator de Impacto: 7.324)

DEDICATÓRIA

Dedico à eterna Prof. Dra. Mirela Jobim de Azevedo (in memoriam), por ter sido uma grande fonte de inspiração e exemplo de mulher, professora e profissional íntegra e ética, sendo respeitada, amada e jamais esquecida.

Dedico aos meus pais, cujo empenho em me educar sempre veio em primeiro lugar. Aqui estão os resultados dos seus esforços também.

"A verdadeira motivação vem de realização, desenvolvimento pessoal, satisfação no trabalho e reconhecimento" (Frederick Herzberg)

AGRADECIMENTOS

À toda Equipe de Nutrologia do Hospital de Clínicas de Porto Alegre, pelo apoio e atenção prestados para o andamento desta pesquisa.

À Prof. Dra. Luciana e Prof. Dra. Maria Helena por acreditarem no desenvolvimento deste projeto, e por toda a orientação prestada nestes últimos anos, que foi indispensável para o meu desenvolvimento como aluna e profissional.

Às minhas queridas colegas nutricionistas que fizeram parte deste trabalho, Carla e Ana Jaqueline, que com o pontapé inicial tornaram possível a realização desta publicação.

E aos meus familiares e amigos próximos pela compreensão, paciência e auxílio de todas as formas, vocês foram primordiais por me acompanhar diariamente neste processo, possibilitando que a execução desta dissertação fosse realizada calmamente.

SUMÁRIO

LISTA GERAL DE ABREVIATURAS

HIV – Human Immunodeficiency Virus

AIDS – Acquired Immunodeficiency Syndrome

CDC – Center for Disease Control and Prevention

HAART – Highly Active Antiretroviral Therapy

BMI - Body Mass Index

NRS-2002 – Nutritional Risk Screening

CCI – Charlson Comorbidity Index

CC – Calf Circumference

HGF – Hand Grip Force

ESPEN – European Society of Parenteral and Enteral Nutrition

ASPEN – American Society of Parenteral and Enteral Nutrition

PVHIV – Pessoas Vivendo com HIV

TARV – Terapia Antirretroviral

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RESUMO

Introdução: O estado nutricional prejudicado e a má adesão ao tratamento antirretroviral, corroboram para o aumento no risco de desenvolvimento de doenças graves e desfechos negativos em pacientes com HIV/SIDA. Analisamos a frequência de desnutrição e seus fatores associados e a possível associação do estado nutricional com tempo de internação hospitalar e mortalidade em pacientes internados em um hospital terciário no sul do Brasil.

Métodos: Estudo de coorte prospectivo com pessoas vivendo com HIV (PVHIV), maiores de 18 anos, em consultoria com a equipe de infectologia do Hospital de Clínicas de Porto Alegre, avaliados para parâmetros nutricionais e antropométricos em até 72 horas após a admissão e acompanhados por um ano para análise dos desfechos.

Resultados: Foram triados 613 pacientes e 243 foram incluídos no estudo (53,7% homens, 45,1 ± 12,1 anos, IMC 22,5 ± 4,9 kg/m², CCI 7,6 ± 1,8). Com base no peso usual, 77,8% relataram perda de peso não intencional e 44% uma diminuição maior do que 10% em uma mediana de 5 (IQR 1 - 5) semanas. Houve uma alta prevalência na redução da força de preensão palmar entre todos os pacientes incluídos. Hipoalbuminemia foi encontrada em 47,1% da amostra e aqueles desnutridos apresentaram menores níveis de hemoglobina, IMC, circunferência da panturrilha e maior perda de massa muscular e escore de risco nutricional do que aqueles bem nutridos. Foram 50,3% dos pacientes que necessitaram de readmissões, sendo aqueles que tinham um CCI mais alto e anemia. Houve mortalidade de 18,1% em toda amostra, não havendo diferença significativa entre nutridos e desnutridos, porém, nas análises multivariadas, CCI, circunferência da panturrilha e hipoalbuminemia estiveram associados a maior probabilidade de óbito [OR 1,4; IC de 95% 1,2-1,8 (p = 0,000)], [OR 0,9; IC 95% 0,8-0,9 (p = 0,020)], [OR 3,9; IC95% 2 e 7,8 (p = 0,000)], respectivamente.

Conclusão: A desnutrição foi altamente prevalente em pacientes com SIDA em nosso hospital. As taxas de mortalidade e readmissão foram associadas a menor força e massa muscular.

CAPÍTULO I

1. INTRODUÇÃO

Foi entre 1977 e 1978 que houve os primeiros registros de casos de uma nova infecção com múltiplos sintomas, identificados primeiramente em homossexuais, hemofílicos, haitianos, usuários de heroína injetável e profissionais do sexo. Alvo de grandes preconceitos, a doença passou a chamar a atenção das autoridades e em 1982 foi reconhecido a forma de transmissão através da exposição ao sangue contaminado. Apenas em 1985 foi descoberto que a SIDA (Síndrome da Imunodeficiência Adquirida) seria a fase final de uma doença causada por um retrovírus que então se denominou HIV *(Human Immunodeficiency Virus)*.[1] Uma vez infectado, o indivíduo passa a conviver com o vírus até o fim de sua vida, pois apesar dos avanços na ciência e a evolução de medicamentos que combatem a replicação viral no organismo, transformando o que antes era uma infecção fatal em uma condição crônica tratável através da TARV (Terapia Antirretroviral), não há uma cura[2], porém continuam a melhorar o manejo clínico e o desfecho para indivíduos em risco e vivendo com HIV[3].

O uso regular da TARV, possibilita tornar o vírus indetectável e, a partir disso, o estudo PARTNER[4], de 2018 confirma a intransmissibilidade do vírus quando carga viral não é detectável, apoiando a campanha mundial I = I (indetectável = intransmissível). Porém, a má adesão ao tratamento corrobora para um agravo do sistema imunológico, tornando o indivíduo suscetível ao aparecimento de doenças oportunistas e o desenvolvimento da Síndrome de *Wasting*, podendo levar a desnutrição[5].

No Brasil, o número de novos casos e de mortes de HIV/SIDA vem caindo desde a implementação da Lei nº 9.313, de 13 de novembro de 1996, que garante o acesso universal ao tratamento com a TARV, sendo disponibilizada pelo Sistema Único de Saúde (SUS).[6] Embora seja uma política pública positiva, as estatísticas ainda são preocupantes e o Rio Grande do Sul é o terceiro estado brasileiro com a maior taxa de detecção do HIV (28,3/100.000 habitantes) e, entre todas as capitais, Porto Alegre apresenta o maior coeficiente de transmissibilidade (58,5/100.000 habitantes), e mortalidade (22,0 óbitos/100.000 habitantes) do país.[7]

O estado nutricional do paciente está fortemente relacionado ao HIV, já que a deficiência imunológica resultante de HIV leva à desnutrição, e a desnutrição leva à deficiência imunológica, contribuindo para uma progressão mais rápida para a SIDA[8]. A desnutrição foi uma das primeiras complicações da SIDA a ser identificada e um dos diagnósticos mais frequentes na população infectada pelo HIV[9]. Ela se dá pela ingestão insuficiente de alimentos, má absorção de nutrientes, desordem metabólica e infecções recorrentes e crônicas, impactando em uma redução de massa muscular, anorexia e diarreia, progredindo de uma condição aguda para crônica.[10] Nessa população, mesmo a perda de peso inferior a 5% do peso corporal total está associada à progressão da doença e consequentemente piores desfechos.[11]

O diagnóstico e tratamento nutricional ganha cada vez mais destaque e relevância, visto que há uma diversidade de sinais e sintomas que impactarão na qualidade de vida daqueles que vivem com o vírus[12], sendo imprescindível a individualização para se definir a melhor terapêutica e conduta clínica, com foco em reduzir agravos e controlar fatores de risco.[13] De acordo com Soltani et al, três a cada cinco pacientes hospitalizados tem um maior risco nutricional, estando associado ao aumento da mortalidade.[14] Embora exista uma mudança no padrão de composição corporal nestes pacientes nos últimos anos, passando de um perfil de baixo IMC, para a eutrofia e até mesmo o excesso de peso, a desnutrição ainda persiste.[15] Nesse contexto, o objetivo do nosso estudo foi avaliar a frequência de desnutrição e seus fatores associados, e a possível associação entre estado nutricional e tempo de internação e mortalidade em pacientes adultos vivendo com HIV/SIDA internados no Hospital de Clínicas de Porto Alegre, em consultoria com a equipe de Infectologia HIV.

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CAPÍTULO II – ARTIGO ORIGINAL

2.1 ABSTRACT

Background: Patients who are treating HIV/AIDS with poor nutritional status and low adherence to treatment have high risks to develop serious diseases and negative outcomes. We aimed to analyze the frequency of malnutrition and its associated factors and the possible association of nutritional status with hospitalization length of stay and mortality. *Methods:* Prospective cohort study (one-year follow-up) of HIV/AIDS patients evaluated by the infectious disease team of a tertiary hospital in Southern Brazil. *Results:* 243 patients were included in the study (53.7% man, 45.1 ± 12.1 years, BMI 22.5 ± 4.9 kg/m^2, CCI 7.6 ± 1.8), and malnutrition prevalence was 43.2%. Based on usual weight, 77.8% reported unintentional weight loss and 34.2% decrease greater than 10% with a median of 5 (IQR 1–5) weeks. Malnourished patients had lower hemoglobin, BMI, calf circumference levels, and a greater loss of muscle mass and nutritional risk score than the well-nourished. Overall, 50.3% required readmission and there was a total mortality of 18%, with no significant difference between nourished and malnourished. In multivariate analyses, lower calf circumference mass (mortality OR 0.9) was associated with adverse outcomes after adjustment for severity scores and enteral nutritional support was associated with readmission (OR 1.5) but not with overall mortality. *Conclusions:* Malnutrition was highly prevalent in patients with AIDS in our hospital. Mortality and readmission rates were associated with lower strength and muscle mass.

Keywords

"HIV Nutritional Status"; "Acquired Immunodeficiency Syndrome"; "Weight Loss";

2.2 INTRODUCTION

Infection by the Human Immunodeficiency Virus (HIV) is a significant public health problem worldwide. Latin America is considered the third most affected global region, in which about a quarter of individuals with HIV do not know their diagnosis and 40% do not have access to antiretroviral therapy[1]. In Brazil, by the end of 2018, 66% of people living with HIV in the country were receiving antiretroviral therapy[2], and according to the HIV/AIDS Epidemiological Bulletin of the Brazilian Ministry of Health published in 2020, 41,909 new cases were diagnosed (17.8/100,000 inhabitants), 37,308 cases of Acquired Immunodeficiency Syndrome (AIDS) were declared and a total of 10565 deaths caused by AIDS (4.1/100,000 inhabitants). Compared to 2012 these numbers had a reduction of 16.8% in the detection rate and 22.8% in the mortality rate, possibly caused by the implementation of social programs by the Federal Government such as "Treatment for All"[3]. Rio Grande do Sul is the third Brazilian state with the highest HIV detection rate and among all the capitals, Porto Alegre has the highest coefficient of transmissibility and mortality in the country[4].

Malnutrition was one of the first identified complications of AIDS and it was one of the most common diagnoses in the HIV-infected population in the past[5]. The Centers for Disease Control and Prevention (CDC) defined in 1987 as "wasting syndrome" characterized by involuntary weight loss (greater than 10%), chronic diarrhea or fever for more than 30 days associated with weakness (asthenia). Muscle and adipose tissue loss also lead to inability to perform daily activities resulting in social isolation, depression, and poor adherence to treatment[6]. Although Brazil is one of the first countries that prioritized the free distribution of Highly Active Antiretroviral Therapy (HAART), controlling the course of the disease and providing better survival[7], weight loss and malnutrition continue to be a common problem for certain subgroups infected by HIV, such as those with late-diagnose late and those with failed or non-adherent antiretroviral regimens[8].

Body mass index (BMI) is an essential tool to identify the nutritional status in hospitalized patients with HIV[9]. Weight loss is considered an independent predictor of mortality in HIV-infected individuals in malnourished patients (BMI 18.5 – 17 kg/m²), especially if moderate (BMI 16.99 – 16 kg/m²) to severe (BMI <16 kg/m²)[10]. Weight loss

or decreased BMI continues to be predictive of opportunistic and/or AIDS-related infections[5], and a decline in therapeutic response. In HIV-infected patients, even weight loss of less than 5% of total body weight is associated with disease progression, emergence of opportunistic infections and increased mortality[11].

In a 2008 cohort study in Africa, with 320 patients who started antiretroviral therapy, an increase in mortality was observed with a reduction in BMI, and the estimated mortality rate in one year for patients with adequate nutritional status was 13%, those with severe to moderate malnutrition presented 21% of mortality rate, and severe malnutrition 46.8%[12]. Later, in a Brazilian cross-sectional study, the mortality was higher in patients with lower BMI (22% in BMI <16 kg/m² vs. 12% in BMI <18.5kg/m²)[6]. These data highlight the need for urgent nutritional studies in patients living with HIV, particularly in developing countries where malnutrition is often a result of poverty and food insecurity[12] associated with the disease.

Therefore, this study aims to evaluate the frequency of malnutrition and its associated factors and the possible association of nutritional status and hospitalization length of stay and mortality in adult patients living with HIV/AIDS hospitalized in a tertiary hospital in the Southern Brazil.

2.3 MATERIALS AND METHODS

A cohort study was conducted, with patients older than 18 years old, diagnosed with HIV/AIDS, admitted from August 2017 to March 2020, at the Hospital de Clínicas de Porto Alegre/RS, Brazil, a tertiary teaching hospital, which has 642 beds and a reference service for patients with HIV. Patients who were hospitalized directly in the intensive care unit, those with impaired communication and pregnant women were excluded. Two equally trained nutritionists performed the screening and inclusion of patients with HIV supported by infectious diseases team (RG, AJN).

All participants signed the informed consent form, then, they were evaluated in order to obtain clinical, functional, and anthropometric data, and all the information was taken in a standard form, as the physical assessment and functional capacity, within 72 hours after admission to the clinical ward. Information on the reason for the current

hospitalization, HIV duration (diagnosis until hospitalization), antiretroviral therapy, and existence of coinfections, alcohol or drug use was obtained the each patient's electronic record; the Nutritional Risk Screening[13] (NRS-2002) was also performed. Then, the Charlson Comorbidity Index[14] was used as a predictor of mortality due to existing comorbidities.

A brand digital scale from Personal® was used for anthropometric evaluation and the height was measured with the Luft® stadiometer.

Calf circumference (CC) was measured on the left leg, with an inelastic measuring tape, in the most protruding part, and the cutoff point of 31cm was used, as recommended by the European Sarcopenia Consensus. For the measurement of handgrip strength (HGS), the Jamar® hydraulic model dynamometer was used[15], and the cutoff point of 27kgf for men and 16kgf for women were adopted, according to the European Sarcopenia Consensus. When the patients could not perform the dynamometry or presented any injuries in the left leg, these measurements were not performed and recorded as not applicable. For malnutrition classification, the parameter of unintentional weight loss was used for cases with loss higher than 10% and/or BMI less than 18.5 kg/m².

The laboratory analyses included were serum albumin, ferritin, magnesium, serum phosphorus, hemoglobin, hematocrit, CD4 cell count and viral load count, all examinations are usually requested in the clinical care routine and processed in the hospital's pathology laboratory.

The collected data were entered in the Excel program and later exported to the SPSS v.20.0, program for statistical analysis. Categorical variables were described by frequencies and percentages. The quantitative variables with symmetric distribution were described by mean and standard deviation and those with asymmetric distribution by median and interquartile interval. Categorical variables were associated with the Chi-square test. The quantitative variables with symmetric distribution were compared by Student's t-test for independent samples. The variables with asymmetric distribution were compared by the Mann-Whitney test. Sigma Plot was used to perform the correlations of non-parametric variables, with the Spearman test. Multivariate analyses (dependent variable mortality or rehospitalization) were adjusted according to clinical significance or univariate significance of the independent variables. A 5% significance level was established.

2.3.1 Ethics approval

The study protocol was submitted and approved by the Research Ethics Committee of Hospital de Clínicas de Porto Alegre, project number 17-0453. All patients consented to participate in the study.

2.4 RESULTS

2.4.1 *Patient Recruitment*

Out of 613 patients living with HIV/AIDS evaluated by the Infectology-HIV team, we included 243 hospitalized in the ward during the study period (Figure 1). Main reason for exclusion were primary admission into the Intensive Care Unit, Recovery Room or to a unit attached to the hospital, direct discharge from the emergency room, restricted or non-collaborative patients and pregnant or postpartum women.

2.4.2 *Patient Characteristics*

Among the 243 patients included in the study, 53.1% were male, aged 45.5± 12.1 years, 64.6% were self-declared as white and 19.3% were married. Behavioral habits such as drug use were reported by 25.9% of the sample, as well as alcohol (32%) and current smoking (31.3%). About HIV infection duration, 23% discovered their diagnosis for less than one year and the most part of the sample for more than five years. Considering the use of HAART, 16% of patients were going to start or restart their use, and almost half of the sample affirmed not using HAART on a regular basis.

The median CD4 cell count was 201 (IQR 67.5 – 390) cells/mm³, and it was lower than 200 cells/mm³ for 11.1% of all patients included. High viral load (> 100,000 copies) was found in 24.3% and 30.9% had an undetectable viral load (<50 copies). Out of the 148 patients who had detectable results, the median viral load was 21,221 (IQR 269,75 – 255,894.0) copies.

When evaluated by the Charlson Comorbidity Index (CCI), patients had an average of 7.6 ± 1.8 score. Most frequent comorbidities during the current hospitalization were viral hepatitis, pulmonary tuberculosis, and neurotoxoplasmosis, respectively. Regarding

neoplasms, 29.2% had or were diagnosed with, and the most common were non-Hodgkin's lymphoma, Kaposi's sarcoma, and lung cancer.

2.4.3 *Anthropometric and Nutritional Characteristics*

Nutritional evaluation was performed within 72 hours of hospital admission. Most patients were eutrophic (mean BMI 22.5±4.9 kg/m²) and based on their usual weight, 77.8% reported an unintended weight loss [8.4 (IQR 1.8–16.5%)] with 34.2% presenting weight loss greater than 10% over a median of five weeks (IQR 1– 12). Overall, BMI <18.5 kg/m² was found in 21.4% and BMI > 30 kg/m² in 9.9% of the patients. The loss of lean mass was assessed subjectively during the interview and 51% of the patients had an apparent reduction in muscle mass and 16. 5% had edema in the lower and/or upper limbs. Median calf circumference was 31 (IQR 26– 33.5) cm, and 43.2% had a circumference smaller than 31cm. According to the nutritional risk score (NRS-2002) performed on the admission, 39.1% of patients were at high risk of malnutrition during their hospitalization.

2.4.4 *Nutritional Support during Hospitalization*

On the day of the interview, most patients were consuming oral diet and only six (5.3%) received enteral nutrition support, 4.1% had their food suspended due to medical recommendation for tests requiring fasting. By the end of hospitalization, the number of patients receiving enteral nutritionally increased, reaching a total of 27 (9.9%) and two patients were on parenteral nutrition. According to nutrition support prescription, malnourished patients used more enteral nutritional therapy than nourished patients [19 (70.4%) vs. 8 (29.6%) p = 0.003]. Data about oral dietary tolerance or nutrition supplements prescription were not available.

2.4.5 *Malnutrition and Nutrition Patients*

The prevalence of malnutrition (BMI <18.5 kg/m2 and/ or weight loss >10%) was 43.2% in our study. Table 1 summarizes the characteristics of patients with malnutrition compared to well-nourished patients. There was no difference between groups when compared age, type of antiretroviral regimen, duration of infection, and CCI. About the

laboratory analysis, the malnourished ones had lower levels of hemoglobin when compared to the nourished [10.5 ± 2.3 vs. 11.2 ± 2.3 (p=0.043)], and higher values of c-reactive protein [78.1 (22.8 – 186.5) vs. 48.7 (9.9 – 166.8) p=0.036], respectively. Albumin tests were performed in 140 and 47.1% of the patients had hypoalbuminemia.

As expected, patients with malnutrition had significant lower weight, BMI and calf circumference than nourished ones. They also showed a bigger loss of muscle mass and a higher nutritional risk score according to NRS-2002, as shown in the Supplementary Table. Due the standardization of hospital diets, these patients also received a higher caloric [38 (IQR 33–45) vs. 30.7 (IQR 26.1–36.4) p<0.001] and protein intake [1.6 (1.3–2) vs. 1.4 (1.2–1.6) p>0.001] when the offer per kg of weight was evaluated. Regarding the handgrip strength and the cutoff points established by the European Consensus 2019, the prevalence of strength reduction was 74.9% in men and 38% in women. Malnourished individuals showed a significant reduction when compared to the nourished group, as indicated in Table 2. In the multivariate model, calf circumference was associated with a higher probability of malnutrition [OR 0.8; 95%CI 0.8 – 0.9 (p = 0.000)], but statistically, we cannot affirm this association for hand grip strength [OR 0.0; 95%CI 0.9 – 1 (p = 0.052)].

2.4.6 *Follow-up*

Intra-hospital mortality

In-hospital mortality was 6.5% with a median of 33 (16.5 – 47) days of hospitalization. Men died more than women [13 (81.3%) vs. 3 (18.7%) p = 0.020]. Anemia [12 (75%) vs 106 (46.9%), p = 0.037] and hypoalbuminemia [9 (56.2%) vs 57 (53.7%), p = 0.016]) were more frequent in patients who died than survivors. Enteral nutritional therapy was also more frequent in deceased than surviving [6 (37.5%) vs. 18 (7.9%), p<0.001]. According to the handgrip strength, 60.5% of men and 100% of women had lower strength than the established cutoff point, but this result is significant only for women (p=0.029) who died. In the multivariate model, enteral nutritional support and CCI remained associated with a higher probability of death, enteral nutrition [OR 4.9; 95% CI 1.5–16.2 (p=0.008)], and CCI [OR 1.4; 95% CI 1.1–1.8 (p=0.003)].

Hospital Readmission

Out of the 227 living discharged patients, 123 (50.3%) required rehospitalization with a median of 2.5 times (IQR 1–3). Readmissions were found in patients who already had a higher CCI [7.9 ± 1.7 vs 7.1 ± 1.4 (p=0.000)], anemia [52.8% vs 39.4% (p=0.032)] with a lower mean hemoglobin of [10.7 ± 2.3 vs 11.3 ± 2.4 (p=0.047)], and enteral feeding in the previous hospitalization [52.8% vs 0.9% (p=0.032)], but no associations for hospital readmission in multivariate analyses, as we can see on Supplementary Table 4.

Mortality after first hospital discharge

There were 28 deaths after the first hospital discharge, and patients who died had a smaller calf circumference [26 ± 4.5 vs 30.6 ± 5.1 (p = 0.000)], a larger CCI [8.7 ± 1.6 vs 7.3 ± 1.5 (p = 0.000)], anemia [75% vs 42.7% (p = 0.002)] with a mean hemoglobin of [10.1 ± 2.3 vs 11.1 ± 2.3 (p = 0.031)]. Furthermore, these patients showed a significant reduction in handgrip strength [18.2 ± 8.4 vs 22.1 ± 8.9 (p = 0.031)]. In the multivariate analysis adjusted for severity, CCI [OR 1.4; 95% CI 1.1–1.8 (p=0.004)], and calf circumference [OR 0.8; 95% CI 0.7–0.9 (p=0.002)].

Overall mortality

Overall mortality in our study was 18.1% (44 patients). Higher CCI [8 .9 ± 2.2 vs 7.3 ± 1.5 (p = 0.000)], lower hemoglobin [9.9 ± 2.3 vs 11.1 ± 2.3 (p = 0.002)], and higher frequency of hypoalbuminemia [52.2% vs 21.6% (p=0.006)] were observed in deceased patients. Reduction in handgrip strength [18.6 ± 8.4 vs. 22.1 ± 8.9 (p= 0.018)] and lower calf circumference [27.2 ± 5.2 vs. 30.6 ± 5.1 (p = 0.000)] were also found in patients who died. In the multivariate analyses, CCI, calf circumference, and hypoalbuminemia were still associated with a higher probability of death [OR 1.4; 95%CI 1.2–1.8 (p=0.000)], [OR 0.9; 95%CI 0.8–0.9(p=0.020)], [OR 3.9; 95% CI 2–7.8 (p=0.000)], respectively. Neither dynamometry nor low hemoglobin values remained associated with mortality.

2.5 DISCUSSION

The prevalence of malnutrition was 43.2% and overall mortality was 18% with 50.3% hospital readmission in a period of one year of follow-up. Surprisingly, malnutrition (based on BMI<18.5 and/or weight loss greater than 10%) was not associated with higher mortality or rehospitalization; on the other hand, lower calf circumference and lower muscle strength were associated with these outcomes. Also, enteral feeding was associated with intrahospital mortality and readmission but not with overall mortality.

Regarding malnutrition, the prevalence in our studies was similar to other Brazilian studies, as the sample by Souza et al.[16] and Andrade C et al.[6] with 42.5% and 43%, respectively. Most patients in our sample had chronic malnutrition, though, 34.2% referred a significant weight loss in the last few months. Chronic and acute malnutrition may have different effects in patients living with HIV. Wasting syndrome could be identified in 8.2% of our patients (considering involuntary weight loss greater than 10% in four weeks). Although this complication is less prevalent than in the beginning of AIDS-era, it is still a life-threatening complication[17].

Malnourished patients received more calories and protein per kilo than nourished patients, despite the food intake of these patients has not been evaluated, the amounts agree with recommendations from ESPEN[18] and ASPEN[19] guidelines. Also, according to ESPEN guideline, nutritional therapy should be indicated when there is significant weight loss >5% in three months, and we had a sample with >10% in six months of 14.4%, but only 5.3% received enteral support, and by the end of hospitalization increasing to 9.9% and two patients were on parenteral nutrition. Enteral tube feeding in the first hospitalization of the study was associated with in-hospital mortality and readmission in this study. In Veronese's study with older patients, tube feeding was also considered a higher risk of mortality associated with patients with a lower BMI, malnourishment, worse cognitive status, and a greater number of comorbidities, being considered fragile[20].

Sarcopenia is highly prevalent in patients living with HIV. In a recent meta-analysis including 13 studies, in a total of 2,267 participants, 24.1% presented sarcopenia[21]. For its diagnosis, a sequence of tests involving handgrip strength and functional capacity are necessary, according to the review of European Consensus in 2019[22]. This concept evolved

over the years, as in 2010 consensus[23], the handgrip strength test and the verification of muscle mass reduction were enough to diagnose this condition. In our sample, the prevalence of handgrip strength was 74.9% men and 38% women based on 2019 cutoff point. According to a meta-analysis published in 2020, sarcopenia in HIV patients seems to occur earlier, 15 years before the population without HIV[21]. In the same study, it was identified that HIV-positive patients have 6.1 higher chances to develop this condition, and the existence of the virus should be considered a risk factor. Based on the new consensus, we cannot affirm the prevalence of sarcopenia in our sample, but the strength reduction/lower calf circumference were predictors of adverse outcomes in our population.

Calf circumference, another indirect tool for evaluating muscle mass, is indicated in literature as being able to predict hospital readmission in adults[24], and 43.2% of our sample presented a circumference smaller than 31cm—reference value used in the guideline by the European Working Group on Sarcopenia in Older People[22], which also showed a significant correlation with viral load and CD4+ count in the study by Almeida D[34].

We found that most hospitalized patients had a reduction in lean mass and a certain reduction in handgrip strength, thus being classified as high risk of developing sarcopenia, but more tests should be applied to determine this diagnosis. Generally, the patients also had a mean laboratory profile, with high viremia and an impaired immune system as seen by the CD4+ average, in addition to anemia and hypoalbuminemia being predictors of poor nutritional status. Thereby, malnourished patients had a greater need to use nutritional therapy, to avoid further damage to health. Although it is widely known that patients adhering to HAART with periodic monitoring by multidisciplinary teams have a quality of life similar to non-infected people, this part of infected people who need tertiary care should receive even greater attention related to psycho-social issues, in order to understand the conflicts they face and try to find better strategies to ensure regular use of HAART.

HIV patients' in-hospital mortality rate differs according to the country's socioeconomic status: in the United States the mortality rate[25] was only 2.6% compared to 34.8% of Nigerians[26]. In a Brazilian cohort study publish in 2017, the in-hospital mortality rate was 11.6%[27]. In our study we had a lower intra-hospital mortality in the first admission (6.5%) but a similar overall mortality after one year as other studies.

Multiple factors could explain our high mortality and readmission rates, besides nutrition and anthropometric measures. Low adherence to treatment was a major problem in our study. Even with public campaigns and free access to HAART offered by the Unified Health System (SUS), 47.3% of the participants of this study declare inconsistent HAART use, in the same way as Souza C et al.[28] and Betancur et al.[29] sample, and the non-adherence involves several factors, such as stigma, depression, anxiety, alcohol, and drug use[30]. Daily consumption of alcoholic beverages, as well as using illegal drugs and active smoking, is in line with Rego S[31] and Teixeira LS[32], confirming the tendency that people living with the virus tend to keep risky behaviors which can negatively affect their clinical health status[31], considering the modulating effect of these substances on human behavior[33]. This may have contributed to the high rate of readmissions in one year.

Our study has some limitations. Firstly, information collected via electronic records, regarding the patient's food consumption was incomplete or absent, although all patients attended a nutritionist—those at greater risk of malnutrition were frequently followed by this professional—and their diet could be readjusted whenever necessary. The large number of readmissions hampered our intention to have a larger sample of patients, as our study design only addressed those under consultation with the HIV infectious diseases team, so our sample may not represent most hospitalized patients, only those more severely affected by the disease. However, this aspect did not disqualify the discussion of our results. Also, we have limited our sample to hospitalized patients in a public hospital of Brazil, and nutritional and socioeconomic status could have biased our results.

In conclusion, malnutrition was highly prevalent in patients with AIDS in our hospital. Mortality and readmission rates were associated with lower strength and muscle mass. More studies are necessary in the HAART era in developing country to evaluate the effect of measures to improve nutrition and muscle gain/function in this group of patients.

Competing interests

The authors declare no competing interests.

Funding

This work was supported by FIPE - Hospital de Clínicas de Porto Alegre. RG received a Master's scholarship from the Postgraduate Program in Endocrinology, Nutrition, and Metabolism by UFRGS, via Coordination for the Improvement of Higher Education Personnel (CAPES).

Author's contribution

RG Performed the screening, data collection, analysis and writing of the manuscript; AJ Performed screening, data collection and preliminary data analysis; CS wrote the research project in its initially; MH responsible for providing guidance on the technical part of HIV patient research and review; LV data analysis, fundamental writing guidelines, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

Acknowledgements

To Nutrology Service of the Hospital de Clínicas de Porto Alegre, for providing the space and materials for daily use to the researchers.

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CONCLUSÃO

Dentre os pacientes incluídos em nosso estudo, a desnutrição foi um fator prevalente e as taxas de mortalidade e readmissão hospitalar foi associado a menor força e massa muscular. Mais estudos são necessários para avaliarmos se estas taxas se mantem entre todos os internados com diagnóstico de HIV ou apenas naqueles mais acometidos, em consultoria com equipe especializada em infectologia HIV/SIDA.

CONSIDERAÇÕES FINAIS E PERSPECTIVAS FUTURAS

Apesar dos avanços no tratamento desta enfermidade, ainda é notável a necessidade de atenção às pessoas que vivem com o HIV, que por diversos motivos não mantém um acompanhamento clínico regular, tornando-se suscetíveis ao surgimento de doenças oportunistas, síndrome metabólica e desnutrição, resultando em indivíduos cada vez mais fragilizados.

Diante da complexidade da infecção e suas possíveis consequências, o monitoramento do estado nutricional torna-se indispensável para que se possa detectar a presença ou o risco nutricional, assegurando uma intervenção adequada e garantindo uma manutenção ou recuperação deste estado, então sendo possível evitar complicações e desfechos negativos, especialmente daqueles com recorrentes reinternações hospitalares.

O acompanhamento destes pacientes mostrou que aparentemente grande parte havia uma fragilidade e vulnerabilidade social importante, sendo assim, há uma necessidade sobre o maior de entendimento dos profissionais de saúde envolvidos, em como auxiliar essa população que, apesar de ter um livre acesso e possibilidade de tratamento com antirretrovirais e acompanhamento, seja de forma ambulatorial ou em unidades básicas de saúde, não assim o fazem, tendo um acometimento importante e piores prognósticos, buscando auxílio emergencial em fases de maior comprometimento sistêmico.

Este estudo também reforçou a importância da avaliação dos parâmetros musculares (força de preensão palmar e medida de circunferência de panturrilha), que podem ser aplicados a beira leito e que se mostraram importantes preditores de desfechos negativos nesses pacientes.

Mais estudos são necessários, avaliando o papel da nutrição precoce e mais individualizada em pacientes hospitalizados com HIV/AIDS, especialmente os de alto risco nutricional como os aqui avaliados.

TABLES AND FIGURES

Figure 1. Flowchart of included patients in the study.

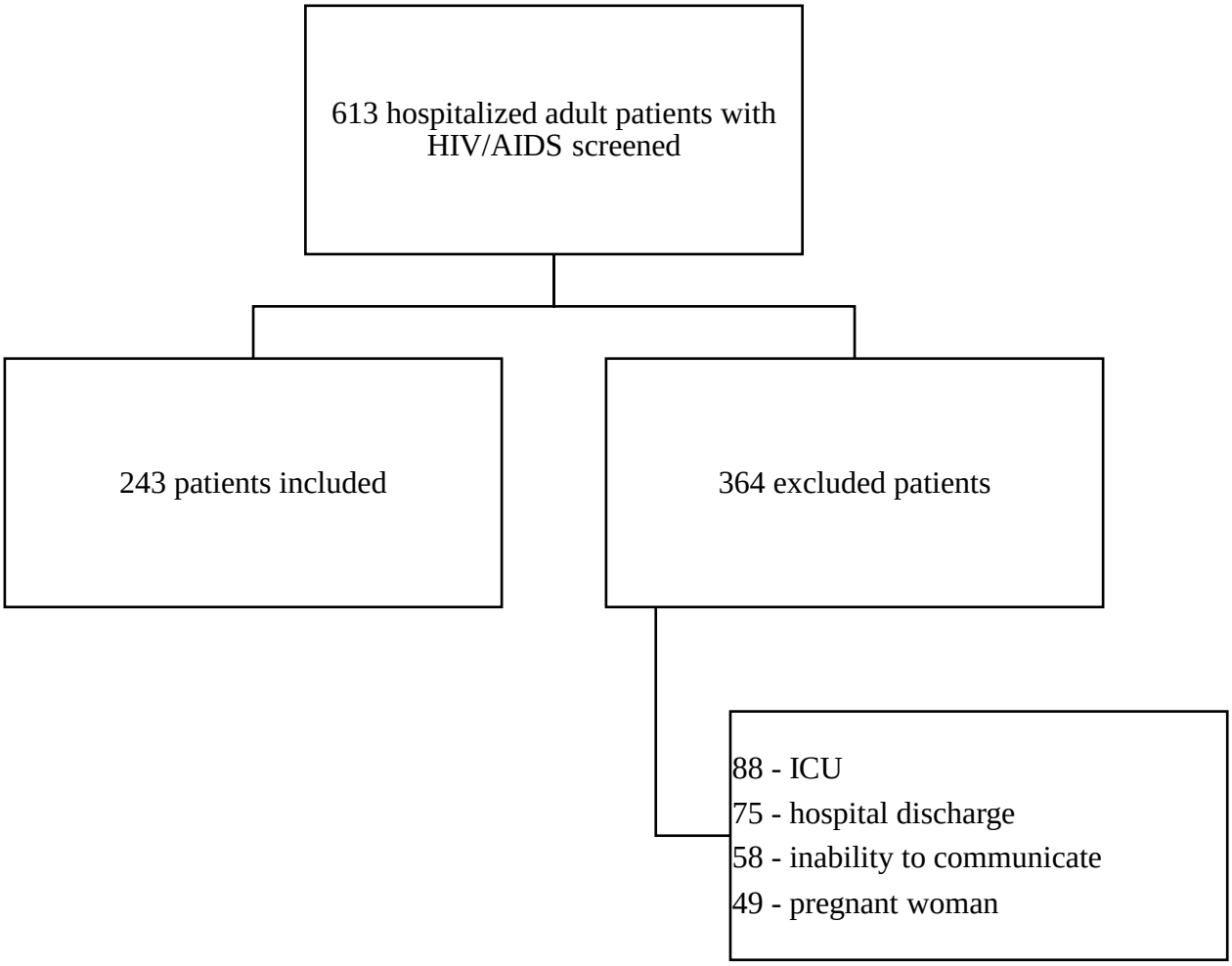

Table 1. Characteristics of nourished vs. malnourished patients.

n= 243	Overall	Nourished (n=139)	Malnourished (n=104)	p-value
Age, Years	45.5 ± 12.1	46.1 ± 12.5	44.8 ± 11.8	0.433
Weight, kg	62.7 ± 15.8	69 ± 13.6	54.1 ± 14.5	0.000
BMI, kg/m²	22.5 ± 4.9	24.9 ± 4.2	19.4 ± 4.0	0.000
Calf Circum., cm (n=220)	31 (26– 33.5)	31.8 ± 4.6	27.7 ± 5.2	0.000
Loss of lean mass (n=124)	124 (51%)	36 (29%)	88 (71%)	<0.001
NRS >3 (n=95)	95 (39.1%)	26 (27.4%)	69 (72.6%)	<0.001
Calories, g/day	34.7 (28 – 40)	30.7 (26.1 – 36.4)	38 (33 – 45)	<0.001
Protein, g/day	1.4 (1.2 – 1.8)	1.4 (1.2 – 1.6)	1.6 (1.3 – 2)	<0.001
CCI	7 ± 1.8	7.8 ± 1.9	7.4 ± 1.6	0.149
CD4 <200 (n=240)	117 (48.1%)	57 (48.7%)	60 (51.3%)	0.091
High Viral Load >100.000	59 (24.3%)	29 (49.2%)	30 (50.8%)	0.210
Detectable Viral Load 100.000 – 51	75 (56%)	43 (59.7%)	32 (51.6%)	0.346
Undetectable Viral Load <50	75 (30.9%)	45 (38.4%)	30 (32.6%)	0.381
Living HIV Infection, years	8 (2 – 16)	9 (2 – 16)	7 (1 – 15)	0.288
Irregular ART use (n=115)	115 (47.3%)	64 (55.7%)	51 (44.3%)	0.923
Drug class				
Non-nucleoside analogs	178 (73.3%)	104 (58.4%)	74 (41.6%)	0.253
Protease inhibitors	17 (7%)	10 (58.8%)	7 (41.2%)	0.888
Nucleoside Analogs	49 (20.2%)	33 (67.3%)	16 (32.7%)	0.105
Lab Tests				
Albumin (n=140)	3.1 ± 0.7	3.2 ± 0.7	3.1 ±0.7	0.649
Ferritin (n=62)	240 (127 – 437)	238 (113 – 442)	242 (132 – 441)	0.245
Cobalamin (n=66)	404.9 ± 206.6	398.1 ± 196.8	412 ± 219.4	0.105
Magnesium (n=151)	1.9 ± 0.2	1.8 ± 0.2	1.8 ± 0.7	0.318
Phosphor (n=84)	3.7 ± 1.1	3.9 ± 1.2	3.5 ± 0.8	0.334
Hemoglobin (n=241)	10.9 ± 2.4	11.2 ± 2.3	10.5 ± 2.3	0.043
Hematocrit (n=239)	32.3 ± 6.7	32.9 ± 6.7	31.6 ± 6.5	0.119
Cholecalciferol (n=7)	26.1 ± 13.2	26 ± 9.1	26.2 ± 15.5	0.115
C- reactive protein (n=174)	67.1 (13.7 – 168)	48.7 (9.9 – 166.8)	78.1 (22.8 – 186.5)	0.036

BMI - body mass index; NRS - Nutritional risk screening; CCI - Charlson Comorbidity Index

Table 1.1 Characteristics of nourished vs. malnourished patients.

n= 243	**Overall**	**Nourished (n=139)**	**Malnourished (n=104)**	**p-value**
Alcohol Consumption	79 (32.5%)	42 (30.2%)	37 (35.5%)	0.699
Drug Use	63 (25.9%)	30 (21.5%)	33 (31.7%)	0.193
Smoking	76 (31.3%)	43 (30.9%)	34 (32.6%)	0.453
Hepatitis	39 (16%)	18 (12.9%)	21 (20.1%)	0.143
Pulmonary Tuberculosis	83 (34.2%)	40 (28.7%)	43 (41.3%)	0.110
Neurotoxoplasmosis	32 (13.2%)	23 (12.9%)	9 (8.6%)	0.065
Non-Hodgkin's Lymphoma	19 (7.8%)	13 (2.1%)	6 5.7%)	0.286
Kaposi's Sarcoma	13 (5.3%)	11 (7.9%)	2 (1.9%)	0.037
Lung Cancer	7 (2.9%)	2 (1.4%)	5 (4.8%)	0.126

Table 2. Hand Grip Strength by Dynamometry.

	Nourished	Malnourished	p-value
GS Woman	20.4 ± 7.2	14.3 ± 7.0	0.000
GS Man	27.4 ± 8.2	21.4 ± 8.7	0.000

GS – Grip strength.

Supplementary Table 1. Mortality by groups in different times.

	In-hospital n = 16			Follow-Up n = 28			Overall n = 44		
	Nourished	Malnourished	p	Nourished	Malnourished	p	Nourished	Malnourished	p
Prevalence	10 (62.5%)	6 (37.5%)		14 (50%)	14 (50%)		24 (54.5%)	20 (45.5%)	
Age, Years	50.4 ± 16.3	50 ± 12.6	0.960	47.2 ± 15	49.2 ± 12.1	0.702	48.5 ± 15.3	49.5 ± 12	0.829
Weight, kg	72.5 ± 14.4	55 ± 17	0.057	63.6 ± 14.7	49.1 ± 14.1	0.013	67.3 ± 14.9	51.1 ± 15	0.001
BMI, kg/m²	25.1 ± 3.8	18.6 ± 6.1	0.021	22.9 ± 3.2	18 ± 4.3	0.002	23.8 ± 3.5	18.2 ± 4.7	< 0.001
Calf Circum., cm	31.7 ± 4.6	25.1 ± 5.7	0.029	26.4 ± 4.9	25.7 ± 4.9	0.700	28.8 ± 5.4	25.5 ± 4.7	0.047
Loss of lean mass	5 (31.2%)	5 (31.2%)	0.182	5 (17.8%)	12 (42.8%)	0.007	10 (22.7%)	17 (38.6%)	0.003
NRS >3	5 (31.2%)	4 (25.1%)	0.515	3 (10.7)	11 (39.2%)	0.002	8 (18.1%)	15 (34.1%)	0.006
Calories, g/day	29.9 ± 13.7	39.7 ± 11.1	0.248	31.3 ± 12.1	35.9 ± 14.6	0.369	32 ± 10.9	37.1 ± 13.4	0.187
Enteral Nutrition	3 (50%)	3 (50%)	0.424	1 (16.7%)	5 (83.3%)	0.065	4 (33.3%)	8 (66.7%)	0.084
CCI	9.8 ± 3.1	8.6 ± 2.9	0.491	8.1 ± 1.8	8.7 ± 1.5	0.914	9.1 ± 2.4	8.7 ± 1.9	0.550
CD4 <200	7 (43.7%)	2 (12.5%)	0.046	6 (21.2%)	8 (28.5%)	0.734	13 (29.5%)	10 (22.7%)	0.765
Viral Load>100,000	2 (12.5%)	0	0.136	3 (10.4%)	2 (7.1%)	0.949	5 (11.3%)	2 (4.5%)	0.648
Irregular ART use	5 (31.5%)	5 (31.5%)	0.202	10 (35.6%)	6 (21.4%)	0.128	15 (34.09%)	11 (25%)	0.766
Hypoalbuminemia	6 (37.5%)	3 (18.7%)	0.658	6 (21.4%)	8 (28.5%)	0.940	12 (27.2%)	11 (25%)	0.714
Anemia	7 (43.7%)	5 (31.2%)	0.551	11 (39.2%)	10 (35.7%)	0.663	18 (40%)	15 (34%)	0.989
Hand Grip Strength by Dynamometry	19.2 ± 10.4	19.3 ± 5.8	0.980	22 ± 7.3	14.4 ± 7.8	0.013	20.9 ± 8.6	15.9 ± 7.5	0.041
Men	23.5 ± 8.8	19.3 ± 5.8	0.344	30.2± 3.3	17.4 ± 7.3	0.030	26.3 ± 7.6	18.2 ± 6.6	0.007
Women	9.2 ± 6.6	-	-	17.5 ± 4.2	9.1 ± 6	0.010	5.9 ± 1.7	9.1 ± 6	0.008

Supplementary Table 2. Difference between dead and survivors.

	In-hospital			Follow-Up			Overall		
	Death (n= 16)	Survivors (n= 227)	p	Death (n= 28)	Survivors (n=199)	p	Death (n= 44)	Survivors (n = 199)	p
Malnourished	6 (5.7%)	99 (94.2%)	0.633	14 (14.1%)	85 (85.8%)	0.467	20 (19%)	85 (80.9%)	0.740
Weight Loss > 10%	3 (8.5%)	32 (91.4%)	0.631	3 (9.3%)	29 (90.6%)	0.557	6 (17.1%)	29 (82.8%)	0.834
BMI < 18.5	4 (7.6%)	48 (92.3%)	0.732	8 (16.6%)	40 (83.3%)	0.311	12 (23%)	40 (76.9%)	0.302
Age, Years	50.2 ± 14.6	45.2 ± 11.9	0.114	48.2 ± 13.4	44.8 ± 11.7	0.154	49 ± 13.7	44.8 ± 11.7	0.040
Weight, kg	66.3 ± 17.1	62.4 ± 15.7	0.347	56.3 ± 16	63.2 ± 15.6	0.030	60 ± 16.9	63.2 ± 15.6	0.213
BMI, kg/m²	22.7 ± 5.6	22.5 ± 4.9	0.895	20.5 ± 4.4	22.8 ± 4.9	0.019	21.3 ± 4.9	22.8 ± 4.9	0.066
Calf Circum., cm	29.1 ± 5.9	30.1 ± 5.2	0.493	26 ± 4.5	30.6 ± 5.1	0.000	27.2 ± 5.2	30.6 ± 5.1	0.000
Loss of lean mass	10 (4.1%)	114 (46.9%)	0.351	17 (14.9%)	97 (85.1%)	0.245	27 (11.1%)	97 (39.9%)	0.137
NRS >3	9 (3.7%)	86 (35.3%)	0.146	14 (16.3)	72 (83.7%)	0.158	23 (9.4%)	72 (29.6%)	0.048
Calories, g/day	35.8 ± 10.2	35.7 ± 25.2	0.982	33,6 ± 13.3	36 ± 26.4	0.644	34.4 ± 12.3	36 ± 26.4	0.702
Enteral Nutrition	6 (2.4%)	18 (7.4%)	0.000	6 (33.3%)	12 (66.7%)	0.005	12 (4.9%)	12 (4.9%)	0.000
CCI	9.3 ± 3	7.5 ± 1.6	0.000	8.7 ± 1.6	7.3 ± 1.5	0.000	8.9 ± 2.2	7.3 ± 1.5	0.000
CD4 <200	9 (3.7%)	108 (44.4%)	0.073	14 (13%)	94 (87%)	0.851	23 (9.4%)	94 (38.6%)	0.582
Viral Load>100000	2 (0.8%)	57 (23.4%)	0.853	5 (8.8%)	52 (91.2%)	0.188	7 (5.2%)	52 (38.8%)	0.207
Irregular ART use	12 (7.7%)	142 (92.2%)	0.449	19 (13.3%)	123 (86.6%)	0.536	31 (20.1%)	123 (79.8%)	0.281
Albumin	2.6 ± 0.5	3.2 ± 0.7	0.010	3.1 ± 0.6	3.2 ± 0.7	0.729	3 ± 0.6	3.2 ± 0.7	0.105
Hemoglobin	9.6 ± 2.3	11.02 ± 2.3	0.027	10.1 ± 2.3	11.1 ± 2.3	0.031	9.9 ± 2.3	11.1 ± 2.3	0.002
Hypoalbuminemia	9 (6.4%)	57 (40.7%)	0.016	14 (24.6%)	43 (75.4%)	0.076	23 (16.4%)	43 (30.7%)	0.006
Anemia	12 (4.9%)	106 (43.6%)	0.037	21 (19.8%)	85 (80.2%)	0.002	33 (13.5%)	85 (34.9%)	0.000
Hand Grip Strength by Dynamometry	19.3 ± 8.7	21.6 ± 8.9	0.304	18.2 ± 8.4	22.1 ± 8.9	0.031	34.4 ± 12.3	36 ± 26.4	0.018

Supplementary Table 3. Readmission

	Yes (n= 123)	No (n= 104)	p
Malnourished	55 (52.3%)	50 (47.6%)	0.631
Weight Loss > 10%	19 (54.2%)	16 (45.7%)	0.639
BMI < 18.5	26 (50%)	26 (50%)	0.893
Age, Years	45.8 ± 12.7	44.5 ± 10.9	0.434
Weight, kg	61.9 ± 15.6	63 ± 15.9	0.576
BMI, kg/m²	22.3 ± 4.8	22.7 ± 5	0.527
Calf Circum., cm	30.1± 5.5	30 ± 4.8	0.877
Loss of lean mass	59 (51.7%)	55 (48.2%)	0.498
NRS >3	46 (53.4%)	40 (46.5%)	0.869
Enteral Nutrition	17 (13.8%)	1 (0.9%)	0.000
CCI	7.9 ± 1.7	7.1 ± 1.4	0.000
CD4 <200	57 (44.5%)	51 (47.2%)	0.199
Viral Load>100000	33 (45.8%)	24 (33.3%)	0.914
Irregular ART use	78 (50.6%)	76 (49.3%)	0.990
Lab Tests	3.2 ± 0.7	3.1 ± 0.7	0.534
Albumin	10.7 ± 2.3	11.3 ± 2.4	0.047
Hypoalbuminemia	34 (59.6%)	23 (40.3%)	0.757
Anemia	65 (52.8%)	41 (39.4%)	0.032
Hand Grip Strength by Dynamometry	20.8 ± 8,6	22.7 ± 9,2	0.106

Supplementary Table 4. Final logistic regression model

Overall mortality (n=44)			
	OR	**95% CI**	**p-value**
CCI	1.48	1.2 – 1.8	0.000
CP	0.90	0.8 – 0.9	0.020
Hypoalbuminemia	3.9	2 – 7.8	0.000
Follow-up mortality (n=28)			
CCI	1.4	1.1 – 1.8	0.004
CP	0.8	0.7 – 0.9	0.002
In-hospital mortality (n=16)			
CCI	1.4		0.000
NE use	4.9		0.008
Readmission (n=125)			
CCI	1.1	0.9 – 1.3	0.266
NE Use	1.5	0.4 - 5	0.444
Albumin	1.6	0.9 – 2.8	0.063
Malnourished (n= 104)			
Calf Circumference	0.8	0.8 – 0.9	0.000
Hand Grip Strength	0.9	0.9 – 1	0.052