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The Impact of Undernutrition Risk on Rehabilitation Outcomes in Ischemic Stroke Survivors: A Hospital-Based Study

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HIGHLIGHTS

- Ischemic stroke survivors (ISS) at undernutrition risk (UR) are more likely to be bedridden.
- UR exacerbates neurological deficits in stroke survivors.
- ISS facing UR have a higher mortality rate.

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ABSTRACT

Patients experiencing a cerebrovascular event are vulnerable to declining nutritional status, hindering rehabilitation. This study aims to analyze the association between malnutrition risk and hospital rehabilitation indicators in ischemic stroke survivors (ISS). This analytical study examined medical records of 160 adult patients (69.3 ± 13 years). Undernutrition risk (UR; independent variable) and rehabilitation indicators (dependent variables) like hospital stay, clinical outcome, functionality, stroke severity, food intake, mobility (bedridden), mechanical ventilation, and enteral nutrition were assessed. Data were dichotomized, and the chi-square test identified associations ($p \le 0.05$), followed by Poisson regression for prevalence ratios. Patients at UR had 2-fold higher risk of death (95% confidence interval [CI], 0.99–4.79), 1.8-fold higher risk of high stroke severity (95% CI, 1.06–3.11), 76% higher chance of being bedridden (95% CI, 1.28–2.44), and 3-fold higher risk of mechanical ventilation (95% CI, 1.20–9.52). UR in hospitalized ISS is associated with deteriorating rehabilitation indicators, including mobility, decreased food intake, mechanical ventilation use, and neurological deficit, indicating an increased mortality risk post-stroke.

Keywords: Cerebrovascular Disorders; Malnutrition; Stroke Rehabilitation; Hospital Medicine

INTRODUCTION

Stroke, a prevalent medical emergency, presents a formidable challenge due to its potential for long-term disability or fatal outcomes [1]. The aftermath of a stroke extends beyond neurological deficits, with ischemic stroke survivors (ISS) frequently grappling with undernutrition as a consequential issue [2]. Defined as an insufficient intake or absorption of nutrients, undernutrition emerges as a significant complication in ISS, hindering the recovery process [3]. This nutritional deficit manifests in various ways, contributing to reduced muscle strength, compromised immune function, and delayed wound healing, thereby impeding the restoration of independence and functionality for ISS [4].

Conflict of Interest
The authors have no potential conflicts of interest to disclose.

Author Contributions
Conceptualization: Pereira DFC, Casonatto J; Data curation: Pereira DFC, Casonatto J, Parron Fernandes KB, Aguiar AF; Formal analysis: Pereira DFC, Casonatto J; Investigation: Parron Fernandes KB, Aguiar AF; Writing - original draft: Pereira DFC, Casonatto J; Writing - review & editing: Pereira DFC, Casonatto J, Parron Fernandes KB, Aguiar AF.

Moreover, bedridden stroke patients often contend with pressure sores as a common complication [5]. The nexus between undernutrition and pressure sores is evident, as undernutrition not only diminishes skin integrity but also retards wound healing, amplifying the risk of pain, infections, and prolonged hospital stays [6,7]. Additionally, undernutrition precipitates muscle weakness, dizziness, and fatigue, heightening the vulnerability of ISS to falls [8]. These falls, in turn, can lead to fractures and other injuries, further complicating the recovery trajectory [9].

Despite the wealth of information available on the consequences of undernutrition in ISS, scant attention has been directed toward the nuanced exploration of undernutrition risk (UR). Defined as a pre-existing condition that may culminate in definitive undernutrition, UR evaluation emerges as a crucial facet of hospital care, especially for patients predisposed to this nutritional challenge [10]. Assessment involves a comprehensive evaluation of a patient's nutritional status, dietary intake, and pertinent medical history, aiming to identify factors heightening their susceptibility to UR [10].

Recognizing stroke as a substantial economic burden on individuals, families, and society at large [11], it becomes imperative to grasp the intricate interplay between UR and stroke-related complications. Elevated UR not only prolongs hospital stays but also escalates the risk of complications, potentially resulting in long-term disability and increased economic burdens associated with stroke care. Thus, our study aims to shed light on the association between UR and various indicators of hospital rehabilitation in ISS. Specifically, we seek to explore the correlation between UR and outcomes such as the length of hospital stay, utilization of enteral nutrition, proficiency in activities of daily living (ADL), mobility (bedridden status), non-invasive mechanical ventilation (NIMV) usage, neurological deficits, and mortality.

MATERIALS AND METHODS

This is an analytical study based on electronic medical record data (**Fig. 1**) from ISS hospitalized patients in a tertiary hospital located in a city of approximately 600,000 inhabitants in the southern region of Brazil (Londrina-Paraná).

Participants

A total of 160 adult patients (> 18 years), both sexes, hospitalized for stroke event were examined. Patients were retrospectively screened from a tertiary hospital between January to December 2021. All patients were admitted to the Emergency Department and underwent nutritional assessment within 72 hours. Patients with incomplete data and/or diagnosis of hemorrhagic stroke and patients without confirmed diagnosis of stroke were excluded from the study (**Fig. 1**).

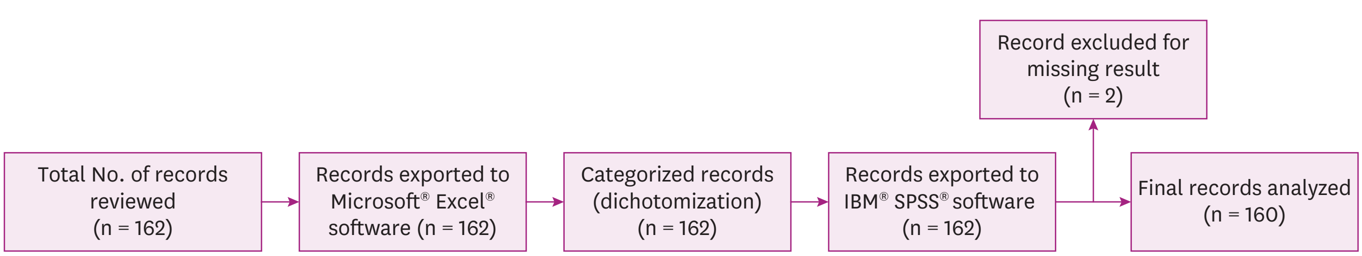

Fig. 1. Data flowchart.

The research protocol was based on the ethical principles established by the National Health Council/Ministry of Health Resolution No. 466/12, which follows the guidelines of the Helsinki Declaration, and was approved by the Institutional Committee on Ethics and Research Involving Human Beings (No. 4.903.486/2021).

Independet variable

The Nutritional Risk Screening tool (NRS-2002) was utilized to assess the nutritional risk in our study [12]. NRS-2002 is widely recognized as the standard in nutritional risk analysis [13]. This tool is designed to evaluate the nutritional status of individuals, providing a comprehensive assessment based on various criteria.

The scoring system of NRS-2002 involves the consideration of different parameters, such as weight loss, body mass index, food intake, and severity of disease. Each parameter is assigned a specific score, and the cumulative score determines the overall nutritional risk. The cut-off points recommended by the NRS-2002 tool for the classification of nutritional risk were adopted in our study, with a threshold of ≥ 3 points indicating a heightened risk.

Dependent variables

The length of hospital stay was obtained by counting the days from admission to discharge/death. The process of dichotomizing this variable was performed using the quartile method, so that individuals with a length of hospital stay greater than 7 days (quartile 4) were classified as "long hospital stay". The clinical outcome was classified as "discharge" or "death". This data was collected through electronic medical records.

Food intake was evaluated by a standardized nutritional assessment applied by a nutrition team, which recorded qualitative and quantitative information on the patient's food intake over the last 15 days. The standardized nutritional assessment was based on Budiningsari et al., [14]. Dichotomization was established as "maintenance" or "reduction" of food intake. Mobility was evaluated through an assessment of the patient's current functional status in three categories: normal gait, partial gait, and bedridden. In this study, the conditions "normal gait" and "partial gait" were classified as "non-bedridden".

Patients who required NIMV were classified. The dichotomization of this variable was "yes" or "no". No patient required invasive mechanical ventilation. Enteral nutrition was characterized by the need for the administration of nutrients directly into the gastrointestinal tract through a tube inserted through the nose, mouth, or abdomen, which reaches the stomach or intestines. The dichotomization of this variable was "yes" or "no".

The Modified Rankin Scale (mRS) was utilized to evaluate the ability to perform ADL [15]. During the dichotomization process, patients were categorized into two groups based on their mRS score: those with scores of 0–2 were considered to have a favorable functional outcome, while those with scores greater than 2 were classified as having disability.

The stroke severity was assessing by the National Institutes of Health Stroke Scale (NIHSS) [16]. The scale consists of 15 items that assess various neurological functions, such as level of consciousness, visual fields, motor function, sensory function, speech, and language. Each item is scored on a scale of 0–4 or 0–3, with a total possible score ranging from 0 (no neurological deficit) to 42 (severe neurological deficit). The process of dichotomizing this

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variable was performed using the quartile method, so that individuals with a NIHSS score greater than 10 (quartile 4) were classified as "high neurological deficit".

Regarding the temporal determination of dependent variables, subjects who were bedridden during hospitalization were considered as such. The variable "food intake decrease" was assessed up to 48 hours before discharge/death. Participants who did not use NIMV during hospitalization were categorized as "no" use. Neurological deficit (NIHSS) was evaluated up to 48 hours before the patient's discharge/death. Patients who used enteral nutrition throughout the hospital stay were classified as "yes." Finally, ADL (Rankin) were assessed up to 48 hours before the patient's discharge/death.

Statistical analysis

Following analysis of data distribution using the Kolmogorov-Smirnov test, a comparison of the data presented in **Tables 1** and **2**, which describes the general characteristics, was performed using an independent t-test. The chi-square test was applied to evaluate the associations between the independent variable UR and all dependent variables. The degree of association was estimated using Phi. Variables that achieved a significance level of $p < 0.05$ were submitted to Poisson regression (PR) analysis to determine the magnitude of the associations between the independent variable and dependent variables (prevalence ratio [PR] and 95% confidence interval [CI]). The data for central tendency and dispersion are presented as mean and standard deviation, respectively. A $p \leq 0.05$ was considered statistically significant. All data were analyzed using the Statistical Packages for Social Sciences software version 20.0 (IBM Corp., Armonk, NY, USA).

RESULTS

The general characteristics of the sample are presented in **Tables 1** and **2**. The evaluated patients (n = 160) had an average length of hospital stay of 6.5 days. There were no significant differences between males and females in terms of age and length of hospital stay.

Table 1. General characteristics of the sample

Numerical variables	No.	Range	Minimum	Maximum	Mean ± SD	t	p value
Age (yr)						−1.398	0.164
Male	85	58	38	96	68.0 ± 12.1		
Female	75	60	39	99	70.8 ± 13.9		
Length of hospital stay (days)						1.535	0.127
Male	85	28	1	28	7.0 ± 5.1		
Female	75	20	2	22	5.9 ± 3.8		
Neurological deficit (NIHSS-score)						−1.778	0.077
Male	85	17	0	17	6.04 ± 5.00		
Female	75	23	0	23	7.51 ± 5.46		

SD, standard deviation; NIHSS, National Institutes of Health Stroke Scale.

Table 2. Functional status

Categorical variable	No.	No symptoms	No disability	Mild disability	Moderate disability	Severe disability
Functional status (Rankin scale)						
Male	85	65 (76.5)	12 (14.1)	1 (1.2)	6 (7.1)	1 (1.2)
Female	75	50 (66.7)	11 (14.7)	7 (9.3)	5 (6.7)	2 (2.7)

Values are presented as number (%).

In **Table 3**, the analyses considering the UR as an independent variable are presented. It can be observed that of the 41 patients with UR, 22% (n = 9) had a fatal outcome, while the rate was 10% among those without the UR (p = 0.05). In **Fig. 2**, the Poisson regression analysis revealed that patients with UR had twice the chance of dying (PR, 2.17 [95% CI, 0.98–4.79]).

Table 3. Association between undernutrition risk and variables related to the clinical condition of hospitalized ischemic stroke survivors

Variables	Undernutrition risk		Chi-square test		Phi	
	Yes	No	χ^2	p value	Value	p value
Clinical outcome			3.766	**0.05**	0.153	**0.05**
Discharge	32 (78.0)	107 (89.9)				
Death	9 (22.0)	12 (10.1)				
Total	41 (100.0)	119 (100.0)				
Bedridden			10.046	**< 0.01**	−0.251	**< 0.01**
Yes	27 (65.9)	44 (37.3)				
No	14 (34.1)	74 (62.7)				
Total	41 (100.0)	118 (100.0)				
Food intake decrease			6.061	**0.01**	0.195	**0.01**
No	25 (62.5)	97 (81.5)				
Yes	15 (37.5)	22 (18.5)				
Total	40 (100.0)	119 (100.0)				
Non-invasive mechanical ventilation			5.913	**0.01**	0.192	**0.01**
No	34 (82.9)	113 (95.0)				
Yes	7 (17.1)	6 (5.0)				
Total	41 (100.0)	119 (100.0)				
Neurological deficit (NIHSS)			4.459	**0.03**	0.167	**0.03**
Low	26 (63.4)	95 (79.8)				
High	15 (36.6)	24 (20.2)				
Total	41 (100.0)	119 (100.0)				
Length of hospital stay			1.381	0.24	0.093	0.24
≤ 7 days	26 (63.4)	87 (73.1)				
> 7 days	15 (36.6)	32 (26.9)				
Total	41 (100.0)	119 (100.0)				
Enteral nutrition			1.458	0.23	0.095	0.23
No	31 (75.6)	100 (84.0)				
Yes	10 (24.4)	19 (16.0)				
Total	41 (100.0)	119 (100.0)				
Activities of daily living (Rankin)			0.036	0.85	0.015	0.85
Favorable	35 (85.4)	103 (86.6)				
Disability	6 (14.6)	16 (13.4)				
Total	41 (100.0)	119 (100.0)				

Values are presented as number (%). Bold words indicate a statistically significant association.
NIHSS, National Institutes of Health Stroke Scale.

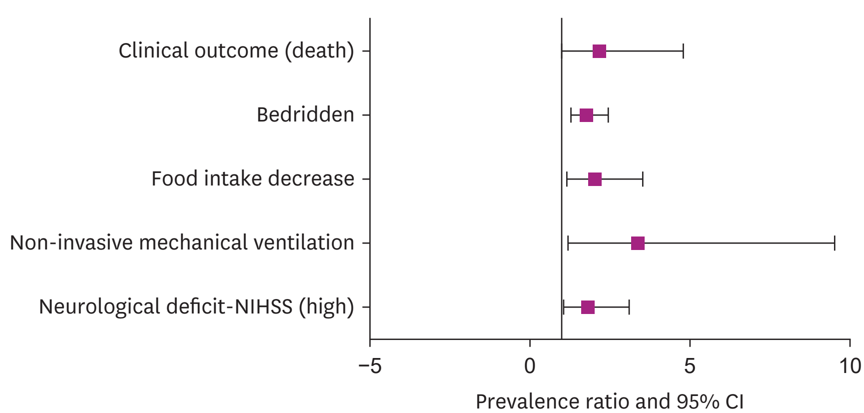

Fig. 2. Regression model between undernutrition risk (independent variable) and clinical outcome (death), mobility (bedridden), food intake decrease, non-invasive mechanical ventilation, and neurological deficit–NIHSS (dependent variables).
NIHSS, National Institutes of Health Stroke Scale.

The risk of malnutrition was also associated with mobility, with 66% of these patients being bedridden, compared to 37% of their peers without the risk of malnutrition ($p < 0.01$). Patients at risk of malnutrition were 76% more likely to be bedridden (PR, 1.76 [95% CI, 1.27–2.43])—as shown in **Fig. 2**. In addition, the UR was associated with a reduction in food intake (37% vs 18%, $p = 0.01$), such that patients at this risk were twice as likely to reduce their food intake (PR, 2.02 [95% CI, 1.16–3.52]) - as shown in **Fig. 2**.

Seventeen percent of patients at UR required NIMV, while only 5% of patients without this risk required this assistance, with a significant association between malnutrition risk and the need for NIMV ($p = 0.01$). In this sense, patients at risk of malnutrition had three times more prevalence of NIMV use (PR, 3.38 [95% CI, 1.20–9.52]).

When analyzing the association between the UR and neurological deficits (NIHSS), it was found that patients without the risk of malnutrition were associated with a lower severity index of stroke compared to those with the risk of malnutrition (80% vs. 63%, $p = 0.03$). Considering the regression analysis (**Fig. 2**), patients with the risk of malnutrition presented an 81% higher chance of having more severe neurological deficits compared to their counterparts without this risk (PR, 1.81 [95% CI, 1.05–3.11]).

There was no significant association observed between the UR and length of hospital stay, use of enteral nutrition, and ability to perform ADL.

DISCUSSION

The current investigation aimed to explore the correlation between UR and diverse variables associated with hospital rehabilitation among individuals who survived ischemic stroke. The findings revealed that individuals who have undergone ischemic stroke and are at UR are at a higher likelihood of encountering decreased food intake, necessitating NIMV, having a greater neurological deficit, being confined to bed, and facing a higher incidence of mortality. While numerous studies have explored these outcomes in cases where undernutrition is already established, there is a paucity of information on the influence of the early stages of UR on these outcomes.

The concepts of undernutrition and UR are closely related but distinct in the field of nutrition. Undernutrition refers to a condition in which an individual's energy and/or nutrient intake is insufficient to meet their metabolic demands, resulting in functional and physiological impairments [17]. The diagnosis of undernutrition is typically established through clinical or biochemical measurements, such as low body weight or serum protein levels. In contrast, UR refers to the likelihood or probability of an individual becoming undernourished in the future due to a variety of factors, including inadequate dietary intake, disease, or aging [18]. To evaluate UR, screening tools such as the NRS-2002 are used [12]. While several studies have investigated the outcomes associated with established undernutrition, research on the impact of UR on these outcomes is limited.

The present study investigated the association between UR and mortality in hospitalized ISS, and found that UR is already linked with an increased risk of mortality compared to ISS without UR. Several mechanisms contribute to this association. Firstly, undernutrition compromises the immune system, rendering individuals more vulnerable to infections and other illnesses [19]. This can further exacerbate their nutritional status and set off a vicious cycle of malnutrition and poor health outcomes. Secondly, undernutrition can result in muscle wasting and loss of strength, which can decrease mobility and increase the risk of falls and other injurie [10]. Thirdly, undernutrition can negatively impact cognitive function, including memory and attention, thereby impairing patients' ability to follow treatment plans and manage their condition effectively [20]. These mechanisms highlight the significance of early identification and intervention for UR in ISS to improve outcomes and prevent negative health consequences.

The current study made an important observation that ISS at UR were more likely to present with severe neurological deficits during hospital rehabilitation. While the precise physiological mechanisms underlying this association are not fully understood, several potential factors have been suggested. One possible explanation is that UR may decrease the supply of glucose and oxygen to the brain, thereby worsening neuronal damage and impeding neurological recovery [21]. Additionally, UR has been linked to elevated inflammation and oxidative stress, both of which can exacerbate neuronal damage and hinder recovery [22]. Furthermore, UR may impact the composition of the gut microbiota, which has been implicated in neurological health. Changes in gut microbiota have been linked to inflammation, oxidative stress, and immune dysfunction, which may contribute to the development of severe neurological deficits in ISS at UR [23]. Therefore, early identification and management of UR in this population may be a critical intervention in improving neurological outcomes and overall health.

The present study findings revealed that ISS at UR have a higher likelihood of being bedridden. UR may lead to significant physical and functional impairments, which can be attributed to several physiological mechanisms. Firstly, UR may exacerbate the inflammatory response in stroke patients, leading to increased production of cytokines and oxidative stress [22]. This may cause tissue damage, impaired wound healing, and decreased muscle strength, ultimately leading to reduced mobility and the need for bedrest. Secondly, UR may lead to decreased muscle mass and function, which may compromise patients' ability to maintain an upright posture and engage in physical activities, leading to deconditioning and immobility [24]. Thirdly, undernutrition may cause anemia, which can decrease the oxygen-carrying capacity of blood, causing fatigue and weakness, and impairing the patient's ability to move around [10]. Therefore, addressing UR in ISS is critical to improving their mobility and overall functional status, which can significantly affect their quality of life.

The present study revealed a notable finding that hospitalized survivors of ischemic stroke with UR had a higher likelihood of requiring NIMV. Several mechanisms could account for this association. Firstly, undernutrition may cause respiratory muscle weakness, leading to inadequate oxygenation and ventilation [24]. Moreover, ischemic stroke-related respiratory dysfunction, such as impaired cough reflex, aspiration, and decreased lung compliance, can exacerbate respiratory distress in undernourished patients [25]. Secondly, undernutrition is linked to systemic inflammation, which may cause lung injury and respiratory failure [26]. Additionally, undernourished ISS are prone to immune dysfunction, increasing the risk of respiratory infections and exacerbating pre-existing respiratory conditions [27]. Lastly, undernutrition is a sign of overall disease severity and may indicate a higher probability of comorbidities, such as heart failure or chronic obstructive pulmonary disease, which can elevate the need for NIMV [28]. Thus, addressing UR in ISS could be crucial to reduce the likelihood of respiratory complications and the need for NIMV.

The present study identified that ISS with UR had a higher likelihood of reducing food intake during hospitalization, as expected. This result may be explained by several factors, including the decreased appetite associated with acute illness, side effects of medications, and the physiological changes that occur in response to stroke [29]. It is important to note that reduced food intake in hospitalized patients can lead to malnutrition and exacerbate existing health problems, including neurological deficits [30]. In light of these findings, healthcare providers should be vigilant in monitoring the nutritional status of ISS with UR and take appropriate steps to ensure that their dietary needs are met during hospitalization to optimize their recovery and reduce the risk of adverse health outcomes.

The current study did not reveal any significant associations between UR and length of hospital stay, use of enteral nutrition, or ability to perform ADL, despite the fact that these variables are important indicators of hospital rehabilitation that are often associated with undernutrition [31-33]. It is possible that UR, as a preceding factor, may not be a significant element in these associations. However, it should be noted that the sample size of the present study, although representative, may not have been sufficient to generate enough statistical power for the analysis of these variables. Future studies with larger sample sizes may be necessary to investigate the relationships between UR and these important outcomes in ISS. Nonetheless, healthcare providers should remain vigilant in monitoring the nutritional status of hospitalized stroke patients to prevent malnutrition and associated adverse outcomes.

This study has some important limitations that must be considered when interpreting the results. Firstly, it is essential to note that the decision-making process for hospital admission is complex and influenced by several factors, including the presence of comorbidities. Consequently, the interpretation of outcomes such as mortality may be challenging due to the intricate nature of biological events. Additionally, the study relies on medical records, which can introduce potential sources of bias. It is crucial to acknowledge that the results presented here are based on an analytical study with limitations, and caution must be exercised when drawing conclusions. However, the study provides important insights into the associations between UR and outcomes in hospitalized patients with ischemic stroke. These findings highlight the need for further research to better understand the impact of UR on these patients' rehabilitation and recovery.

In conclusion, hospitalized survivors of ischemic stroke with UR exhibit a poorer prognosis for hospital rehabilitation, as they are more likely to experience being bedridden, severe neurological deficits, and NIMV. Additionally, they have twice the chance of mortality. These findings emphasize the need to recognize the impact of UR on ISS and incorporate interventions addressing it as part of the rehabilitation process to optimize outcomes.

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