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RISCO NUTRICIONAL EM PACIENTES CRÍTICOS ADMITIDOS NA UNIDADE DE TRATAMENTO INTENSIVO DO HOSPITAL DE CLÍNICAS DE PORTO ALEGRE

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Trabalho de Conclusão de Curso de Graduação apresentado como requisito parcial para obtenção de grau em bacharel em Nutrição, à Universidade Federal do Rio Grande do Sul, Faculdade de Medicina.

Orientadora:
Profª Drª Thais Steemburgo

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RESUMO

INTRODUÇAO: A desnutrição está associada ao maior tempo de internação, maior número de complicações, morbidade e mortalidade em pacientes hospitalizados. Em pacientes críticos de Unidades de Terapia Intensiva (UTIs) o cenário não é diferente e condições como o elevado risco nutricional e perda progressiva de peso são prevalentes nestes pacientes. Os instrumentos de triagem nutricional possibilitam identificar precocemente o risco nutricional e beneficiar os pacientes com uma intervenção nutricional precoce e especializada. Os principais instrumentos para triagem nutricional em pacientes críticos são o Nutritional Risk Screening – 2002 (NRS-2002) e o Nutrition Risk in the Critically Ill (NUTRIC).

OBJETIVOS: (1) Avaliar o risco nutricional através dos instrumentos NRS-2002 e NUTRIC, (2) identificar o desempenho do NUTRIC em relação ao NRS-2002 e (3) identificar as possíveis associações do alto risco nutricional, avaliado por estes instrumentos, com as principais complicações clínicas de pacientes críticos admitidos na UTI.

MÉTODOS: Estudo de coorte prospectivo em pacientes críticos admitidos na UTI do Hospital de Clínicas de Porto Alegre (HCPA). O risco nutricional foi avaliado pelo NRS-2002 e NUTRIC. Como resultado, os pacientes com o escore ≥ 5 pontos foram considerados com alto risco nutricional. Principais dados clínicos foram obtidos por meio dos prontuários eletrônicos. A análise de regressão logística múltipla foi utilizada para calcular razão de chances e seus respectivos intervalos de confiança (95%) para o alto risco nutricional, ajustado para sexo. O grau de concordância entre os instrumentos foi avaliado pelo teste de concordância Kappa. A curva Receiver Operating Characteristic (ROC), construída mediante valores de referência adquiridos pelo NRS-2002, foi utilizada para avaliar o desempenho do NUTRIC.

RESULTADOS: Foram avaliados 200 pacientes críticos (59,4±16,5 anos, 53,5% do sexo feminino). O alto risco nutricional foi identificado em 55% e 36,5% dos pacientes de acordo com o NRS-2002 e NUTRIC, respectivamente. A análise de concordância identificou uma concordância fraca, mas significativa entre os dois

instrumentos (Kappa = 0,192; p = 0,004). O NUTRIC demonstrou um desempenho satisfatório para identificar risco nutricional (área sob a curva ROC 0,697 entre 0,621 – 0,767) em comparação ao NRS-2002. Pacientes com o alto risco nutricional avaliado pelo instrumento NRS-2002, quando comparados aos outros pacientes, demonstraram uma associação significativa com o tempo de internação na UTI (16 vs.14,5 dias; p = 0,050), uso de ventilação mecânica (65,5% vs. 44,4%; p <0,001), presença de infecção (65% vs. 35%, p = 0,004) e óbito (42,7% vs. 27,8%; p = 0,030). Já em pacientes com alto risco nutricional avaliado pelo NUTRIC foram observadas associações significativas com o uso da hemodiálise (64,4% vs. 51,2%; p = 0,003) e óbito (54,8 vs. 25,2%; p <0,001). Em modelo de regressão múltipla, ajustado para sexo, pacientes com alto risco nutricional demonstraram maior risco de uso de ventilação mecânica (51%), presença de infecção (50%), hemodiálise (76%) e óbito (55%).

CONCLUSÃO: O NUTRIC demonstrou bom desempenho na identificação de risco nutricional. O alto risco nutricional foi associado significativamente às complicações clínicas de pacientes críticos internados em UTI.

DESCRITORES: Instrumentos de risco nutricional; NRS-2002; NUTRIC; Pacientes críticos; Unidade de Terapia Intensiva.

ABSTRACT

INTRODUCTION: Malnutrition is associated with prolonged hospital length of stay, greater number of complications, morbidity and mortality in hospitalized patients. In critical patients into Intensive Care Units (ICUs) the scenario isn't different and conditions such as high nutritional risk and progressive weight loss are prevalent in these patients. The nutrition risk screening tools allow to previously identify nutritional risk and benefit patients with an early and specialized nutrition intervention. The main tools used for nutrition risk screening in critically ill patients are the Nutritional Risk Screening – 2002 (NRS-2002) and the Nutrition Risk in the Critically Ill (NUTRIC).

OBJECTIVES: (1) to evaluate nutritional risk through the tools NRS-2002 and NUTRIC, (2) to identify NUTRIC's performance in comparison to Nutrition Risk Screening 2002, and (3) to identify possible associations between high nutritional risk, evaluated by such tools, with the main clinical outcomes of critically ill patients admitted into the ICU.

METHODS: Prospective cohort study in critically ill patients admitted into the ICU of the Hospital de Clínicas de Porto Alegre (HCPA). The nutritional risk was evaluated by NRS-2002 and NUTRIC. As a result, patients with a score ≥ 5 were considered at high nutritional risk. Clinical data were obtained from patients' electronic records. Multiple logistic regression analysis was used to measure the odds ratio and its respective confidence intervals (95%) for high nutritional risk, gender adjusted. The concordance agreement was evaluated through Kappa's coefficient. The Receiver Operating Characteristic (ROC) curve, constructed using reference values acquired by the NRS-2002, was used to evaluate the performance of NUTRIC.

RESULTS: 200 critically ill patients were assessed (59.4 ± 16.5 years old, 53.5% female). High nutritional risk was identified in 55% e 35.6% of the patients, according to NRS-2002 and NUTRIC, respectively. The concordance analysis identified a weak but significant agreement between the instruments (Kappa = 0.192; p=0.004). NUTRIC demonstrated a satisfactory performance in identifying nutritional risk (area on ROC curve 0.697, between 0.621 – 0.767), in contrast with NRS-2002. High

nutritional risk patients assessed by the NRS-2002, when compared to other patients, showed an association with ICU length of stay (16 vs. 14.5 days; p=0.050), use of mechanical ventilation (65.5% vs. 44.4%; p <0.001), presence of infection (65% vs. 35%, p=0.004), and death (42.7% vs. 44.4%; p=0.030). On the other hand, high nutritional risk patients, assessed by the NUTRIC, showed an association with the use of hemodialysis (64.4% vs. 51.2%; p = 0,003) and death (54.8 vs. 25.2%; p <0,001). In a multiple regression model, adjusted for gender, patients with high nutritional risk showed a higher risk of use of mechanical ventilation (51%), presence of infection (50%), renal replacement therapy (76%) and death (55%).

CONCLUSION: The NUTRIC demonstrated good performance in identifying nutritional risk. The high nutritional risk was significantly associated with the clinical outcomes of critically ill ICU patients.

KEYWORDS: Nutrition risk screening tools; NRS-2002; NUTRIC; Critically ill patients; Intensive Care Unit.

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ABREVIAÇÕES

Revisão da Literatura

APACHE II - Acute Physiology and Chronic Health Evaluation II

ASPEN - Sociedade Americana de Nutrição Enteral e Parenteral

DAPEN - Associação Dinamarquesa de Nutrição Parenteral e Enteral

ESPEN - Sociedade Europeia de Nutrição Parenteral e Enteral

HCPA - Hospital de Clínicas de Porto Alegre

IL-6 - Interleucina-6

IMC - índice de Massa Corporal

NRS-2002 - Nutritional Risk Screening – 2002

NUTRIC - Nutrition Risk in the Critically Ill

ROC - Receiver Operating Characteristic

SOFA - Sequential Organ Failure Assessment

UTI - Unidade de Terapia Intensiva

UTIs - Unidades de Terapia Intensiva

SUMÁRIO

1 REVISÃO DA LITERATURA

1.1 DESNUTRIÇÃO: CONCEITO E EPIDEMIOLOGIA NO ÂMBITO HOSPITALAR

Desnutrição é definida como a condição em que ocorre um desequilíbrio energético, proteico e de outros nutrientes, resultando em efeitos adversos nas estruturas dos tecidos e do corpo (STOTTS, 2012). Já o risco nutricional é descrito como o aumento do risco de morbidade e mortalidade da doença de base de um indivíduo devido à presença concomitante de um determinado grau de desnutrição ou inanição (MORETTI, 2014). Conforme Kondrup (2014), o conceito de risco nutricional no contexto de terapia intensiva se refere ao risco de adquirir complicações ou outras formas de desfechos adversos que poderiam ter sido evitados por uma terapia nutricional precoce e adequada (KONDRUP, 2014).

Estudo multicêntrico demonstrou que a desnutrição esteve presente em 48,1% dos pacientes hospitalizados, já a prevalência da desnutrição grave foi de 12,5% nesta população, sendo que grande parte desses doentes desenvolve essa condição durante o período de internação (WAITZBERG; CAIAFFA; CORREIA, 2001). No cenário de Unidades de Tratamento Intensivo (UTIs) esse quadro se mostra ainda mais alarmante, estando a desnutrição presente em 85% dos pacientes criticamente doentes (BARR et al., 2004).

Essa elevada prevalência se deve ao fato de que o estado nutricional dos enfermos críticos piora rapidamente, mesmo quando são admitidos nas Unidades de Tratamento Intensivo (UTIs) em um estado bem nutrido (ISHIBASHI et al., 1998). A desnutrição nestes indivíduos está associada à anorexia, à presença de infecções hospitalares e ao tratamento intensivo, visto que alguns suportes terapêuticos, como a ventilação mecânica e a hemodiálise, estão relacionados à lesão muscular e à depleção proteica (YOUSEFZADEH et al., 2007, BARR et al., 2004).

Além disso, esses pacientes desenvolvem desnutrição em decorrência da resposta inflamatória sistêmica associada à doença crítica e do estado de catabolismo severo causado pelo aumento das citocinas e hormônios relacionados ao estresse (MCCLAVE et al., 2016; JENSEN et al., 2009). Resultados de um estudo clássico demonstraram que pacientes admitidos em uma Unidade de Tratamento Intensivo

(UTI) apresentaram perda de aproximadamente 1-2 kg de proteína corporal (aproximadamente 10-15% do teor inicial de proteína total) durante 10 dias de internação, apesar do bom estado nutricional prévio e do suporte energético e proteico adequado (ISHIBASHI et al., 1998). Essas condições hipermetabólicas diferenciam os pacientes críticos dos demais indivíduos hospitalizados e evidencia a relevância em identificar de forma correta e precoce a presença de risco nutricional nessa população.

1.2 IMPORTÂNCIA DA TRIAGEM NUTRICIONAL

De acordo com a literatura, a desnutrição está relacionada a diversos desfechos clínicos negativos, tais como aumento de morbidade e mortalidade, ocorrência de infecções, hospitalização prolongada e aumento de custos para o sistema de saúde (CORREIA, 2003). A triagem nutricional visa identificar pacientes desnutridos ou em risco nutricional com objetivo de diminuir resultados clínicos desfavoráveis por meio de terapia nutricional especializada (MCCLAVE et al., 2009).

Em um estudo de intervenção prospectivo, 132 pacientes foram triados pelo NRS-2002 com risco nutricional (escore ≥ 3) e, posteriormente, divididos em dois grupos: (I) grupo intervenção, em que os pacientes receberam terapia nutricional agressiva; (II) grupo controle, em que os doentes receberam terapia padrão. O suporte nutricional especializado no grupo intervenção resultou em menores taxas de complicações e readmissões, melhor estado funcional e menor necessidade de antibióticos em relação ao grupo controle (STARKE et al., 2011).

Já em um estudo de coorte prospectivo realizado na China, 1085 pacientes com cirurgia abdominal foram triados quanto ao risco nutricional. Dentre eles, 120 foram classificados como pacientes de risco pelo NRS-2002 (escore ≥ 3). Observou-se que os indivíduos de risco que receberam suporte nutricional especializado antes da operação apresentaram menor período de permanência hospitalar e menor ocorrência de complicações pós-operatórias em relação ao grupo de alto risco sem suporte nutricional agressivo. Essa associação não foi encontrada nos 965 pacientes classificados com baixo risco (JIE et al., 2012).

Rahman et al. (2016), em um estudo observacional, encontrou associação significativa entre adequação nutricional e sobrevivência de 28 dias após admissão na

UTI em pacientes com alto risco nutricional pelo NUTRIC (escore ≥ 5). Nos pacientes de baixo risco, porém, não foi observada essa relação.

Em uma metanálise de 8 ensaios clínicos randomizados, Heyland et al. (2003) demonstrou uma tendência para redução das taxas de mortalidade quando o suporte nutricional foi iniciado dentro das primeiras 48 horas de internação na UTI. Já na metanálise realizada por Doig et al. (2009) uma redução significativa das taxas de mortalidade foi relatada quando a terapia enteral foi iniciada nas primeiras 24h de admissão na UTI. Além disso, a oferta precoce de terapia nutricional reduziu os custos gerais hospitalares (DOIG; CHEVROU-SEVERAC; SIMPSON, 2013).

Esses estudos sugerem que pacientes com alto risco nutricional são mais propensos a se beneficiar de terapia de nutrição especializada do que aqueles com baixo risco. Também demonstram que o suporte nutricional precoce (até 24-48h após a admissão na UTI) está associado a um melhor prognóstico clínico. Identificar o risco nutricional com acurácia e ofertar de forma precoce uma terapia de nutrição agressiva apresenta-se, portanto, como uma estratégia para redução da severidade das doenças e complicações, diminuição no tempo de permanência hospitalar e melhora do prognóstico dos pacientes com alto risco nutricional.

1.3 AVALIAÇÃO DE RISCO NUTRICIONAL EM PACIENTES CRÍTICOS

Identificar o risco nutricional em pacientes criticamente doentes, no entanto, permanece como um desafio para os profissionais da saúde, visto que não são uma população homogênea e não cumprem com os parâmetros de desnutrição tradicionais (MCCLAVE et al., 2009). Os critérios comumente usados para identificar risco nutricional, como exames laboratoriais, exame físico, dados antropométricos, ingestão alimentar e avaliação funcional (KRUIZENGA et al., 2005; FERGUSON et al., 1999; DETSKY et al., 1987; BUZBY et al., 1980), podem não estar disponíveis ou refletir informações errôneas sobre a condição nutricional desses indivíduos.

Isso ocorre porque os pacientes de UTI estão frequentemente sob ventilação mecânica, sedados ou com estado mental alterado, dificultando a obtenção de informações sobre história de ingestão alimentar, estado funcional e sintomas gastrointestinais antes da admissão hospitalar. Já os parâmetros antropométricos, como peso corporal, índice de massa corporal (IMC) e circunferência da cintura e do braço, podem refletir mais alterações no balanço hídrico do que fornecer informações

fidedignas sobre a composição corporal do paciente, uma vez que muitos desses enfermos recebem grandes volumes de fluido com objetivo de manter estabilidade hemodinâmica (MCCLAVE et al., 2009). Com relação ao uso de proteínas séricas como marcadores tradicionais, estas são utilizadas como um reflexo da resposta da fase aguda da doença, não representando com precisão o estado nutricional do indivíduo criticamente doente (JENSEN; WHEELER, 2012, HIESMAYR, 2012).

Além disso, nesses enfermos a gravidade da doença aguda e estresse metabólico contribuem tanto para o risco nutricional quanto o estado nutricional de base (KONDRUP, 2014). As ferramentas tradicionais de avaliação nutricional perdem essencialmente essa interação (HEYLAND et al., 2011), podendo levar a uma classificação equivocada do risco nutricional e ocasionar falhas e atrasos na terapia dessa população.

Diante das limitações expostas, os instrumentos *Nutritional Risk Screening* – 2002 (NRS-2002) e *Nutrition Risk in the Critically* lll (NUTRIC) parecem ser os mais adequados para a triagem de pacientes críticos, visto que são as únicas ferramentas que consideram a condição nutricional do doente concomitantemente ao impacto da sua doença ou trauma sob o estado nutricional (MCCLAVE et al., 2016). O instrumento NUTRIC possui ainda um importante diferencial no contexto de UTIs, dado que todos os seus componentes podem ser obtidos através da revisão do prontuário, sem necessidade de uma entrevista com o paciente ou familiar. Além disso, tanto o NUTRIC quanto a NRS-2002 são sistemas de triagem rápidos, de baixo custo e de fácil aplicabilidade (HEYLAND et al., 2011, KONDRUP, 2003).

O Nutritional Risk Screening – 2002, popularmente conhecido como NRS-2002, foi o primeiro instrumento de triagem de risco nutricional desenvolvido através da medicina baseada em evidências. Essa ferramenta, elaborada pela Associação Dinamarquesa de Nutrição Parenteral e Enteral (DAPEN) e recomendada pela Sociedade Europeia de Nutrição Parenteral e Enteral (ESPEN), foi derivada de uma revisão sistemática de todos os ensaios clínicos randomizados disponíveis na literatura, tendo como objetivo a triagem das características nutricionais dos pacientes em que o suporte nutricional foi efetivo na melhoria de desfechos clínicos. Posteriormente, os estudos clínicos confirmaram sua validade preditiva, demonstrando que a NRS-2002 é capaz de identificar pacientes que se beneficiam de apoio nutricional (JOHANSEN et al., 2004, STARKE et al., 2011). Essa ferramenta é adequada para classificar risco nutricional em todos os enfermos hospitalizados,

independentemente da idade ou da doença. A NRS-2002 classifica o risco nutricional dos indivíduos de acordo com cinco variáveis: (I) perda de peso não intencional nos últimos três meses, (II) apetite, (III) IMC e (IV) fator de estresse da doença. Além disso, (V) a idade acima de 70 anos é considerada como uma variável de risco adicional. A soma da pontuação referente ao estado nutricional com a pontuação referente a gravidade da doença quantifica o risco nutricional dos pacientes, que são classificados como sem risco = 0, baixo risco = 0-1, risco médio = 3-4 e risco elevado ≥5 (KONDRUP, 2003).

Já o escore NUTRIC, validado por Heyland (2011) e recomendado pela Sociedade Americana de Nutrição Enteral e Parenteral (ASPEN), foi elaborado especificamente para quantificar risco nutricional na população criticamente doente e identificar quais pacientes são mais propensos a se beneficiar de uma terapia de nutrição agressiva (HEYLAND et al., 2011, WARREN; MCCARTHY; ROBERTS, 2016). O reconhecimento de que nem todos os pacientes de UTI responderão da mesma forma às intervenções nutricionais foi o principal conceito por trás do escore NUTRIC, já que a maioria das pontuações de risco e ferramentas de avaliação consideram que todos os pacientes críticos estão em alto risco nutricional. Para sua elaboração, identificaram-se as variáveis que possivelmente estariam associadas a mortalidade em uma amostra de 598 pacientes. No modelo final, apenas seis variáveis foram significativamente relacionadas à mortalidade. Esse instrumento classifica os indivíduos de acordo com esses seis critérios: (I) idade, (II) escore Acute Physiology and Chronic Health Evaluation II(APACHE II), (III) escore Sequential Organ Failure Assessment (SOFA), (IV) comorbidades, (V) dias de internação anteriores ao ingresso na UTI e (VI) interleucina 6 (IL-6). Em 2016, Rahman et al. (2016) revalidou a ferramenta excluindo o uso do marcador interleucina 6 (IL-6), visto que não é uma variável comumente disponível no contexto hospitalar (RAHMAN et al., 2016). Para quantificar o risco nutricional, pacientes com pontuação ≥ 6 (quando IL-6 disponível) ou ≥ 5 (quando IL-6 não disponível) são considerados com alto risco.

2 JUSTIFICATIVA

A desnutrição é uma manifestação clínica comum em pacientes hospitalizados e está associada com a maior morbidade e mortalidade hospitalar. Condições como

elevado risco nutricional e perda progressiva de peso são prevalentes em pacientes críticos de Unidades de Terapia Intensiva (UTIs). Os instrumentos de avaliação de risco nutricional possibilitam identificar precocemente o risco nutricional, minimizar a perda de peso e beneficiar os pacientes com uma intervenção nutricional precoce e especializada. Os principais instrumentos de avaliação de risco nutricional em pacientes hospitalizados que consideram a condição nutricional concomitantemente ao impacto da doença ou trauma sob o estado nutricional são os sistemas de pontuação *Nutrition Risk in the Critically Ill* (NUTRIC) e *Nutritional Risk Screening* – 2002 (NRS-2002). Ainda que o instrumento NUTRIC tenha sido particularmente elaborado para triagem de pacientes criticamente doentes, até o momento não existem estudos que comparem se este instrumento tem bom desempenho quando comparado ao NRS-2002, instrumento de referência de triagem nutricional. Ainda, poucos estudos avaliaram a associação do alto risco nutricional, avaliado por estes instrumentos, com as principais complicações clínicas durante o período de internação de pacientes críticos admitidos em uma UTI.

Assim sendo, os principais objetivos desse trabalho são: (1) Avaliar o risco nutricional através dos instrumentos de triagem nutricional: NRS-2002 e NUTRIC, (2) identificar o desempenho do NUTRIC em relação ao instrumento de referência NRS-2002 e (3) identificar as possíveis associações do alto risco nutricional, avaliado por estes instrumentos, com as principais complicações clínicas de pacientes críticos admitidos em uma UTI.

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3 ARTIGO ORIGINAL

Performance of the Nutrition Risk in Critically Ill Compared to Nutritional Risk Screening 2002 and Associations with Clinical Outcomes in Patients Admitted to the Intensive Care Unit.

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Abstract

Background: Nutrition screening tools such as Nutrition Risk of Screening 2002 (NRS-2002) and Nutrition Risk in the Critically Ill (NUTRIC) are available to assess nutritional risk, however, its use in Intensive Care Units (ICUs) is not rigorously studied. The aims of this study are identify the nutritional risk of patients admitted to ICU, to evaluate the performance of NUTRIC in comparison to NRS-2002, and also to identify high nutritional risk and its associations with clinical outcomes of critically ill patients.

Methods: A total of 200 patients in an ICU of a university hospital were included in this retrospective cohort study. Nutritional risk was assessed by NRS-2002 and NUTRIC scores. Patients with score ≥ 5 were considered at high nutritional risk. Clinical data and outcomes measures were obtained from patients' medical records.

Results: The patients had 59.4 ± 16.5 age and 53.5% were female. The high nutritional risk according to NRS-2002 and NUTRIC was 55% and 36.5%, respectively. The concordance analysis identified a weak but significant agreement between the instruments (Kappa = 0.192, p <0.001). NUTRIC demonstrated a satisfactory performance in identifying high nutritional risk (AUC: 0,697; 95% CI 0.621 - 0.767). In multiple logistic regression models, adjusted for gender, patients at high nutritional risk showed increased use of mechanical ventilation (51%), presence of infection (50%), renal replacement therapy (76%), and death (55%).

Conclusion: The NUTRIC tool demonstrated a good performance in identifying risk of malnutrition. A score ≥ 5 was associated with increased risk of clinical outcomes in ICU patients.

Keywords: nutrition screening; critically ill patients; intensive care unit; Nutrition Risk in the Critically Ill; nutritional risk screening 2002.

Introduction

Malnutrition is a frequent condition among hospitalized individuals.[1,2] Such situation is even more prevalent among critically ill patients admitted to the Intensive Care Units (ICUs), considering that they are often in a hypermetabolic state caused by trauma or stress from the acute disease.[3,4] It is known that malnutrition is associated with many bad clinical outcomes, such as the increase in morbidity and mortality, longer hospital stay, and clinical complications.[2,5] Both clinical complications and longer hospital stay promote disease worsening and higher costs for health system.[5]

According to the literature, one of the most effective strategies in the treatment of high nutritional risk patients is the early and specialized nutritional intervention.[6-10] Indeed, identifying the nutritional risk as fast as possible in these patients promote an aggressive and immediate nutritional therapy. Such measure is essential for decreasing adverse events and improving the life quality of these patients during hospitalization.[11]

The nutritional risk identification in critically ill patients is considered a big challenge for healthcare professionals because nutritional screening tools have limitations and specific characteristics. Therefore, it is not well established by international consensus which is the best tool to assess nutritional risk in this population. The *Nutritional Risk Screening 2002* protocol (NRS-2002)[12] and the *Nutrition Risk in the Critically Ill* tool (NUTRIC)[6] seem to be the most adequate tools for screening such patients because they consider the nutritional condition and the impact of the disease or trauma on nutritional status.[13]

Recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN), the NRS-2002 protocol was the first screening tool developed through medicine based in evidence. This tool may be applied to all hospitalized patients and is independent of age or disease. NRS-2002 rates nutritional risk of individuals according to five variables: (I)

unexplained weight loss in the last three months, (II) appetite, (III) body mass index (BMI), and (IV) disease stress factor. Age (V) above 70 years old is considered an additional variable of risk.[12] In patients admitted to an ICU, this instrument identified the high nutritional risk in 40% of the patients.[14] The nutritional risk, evaluated by NRS-2002, was also associated with mortality and longer hospital stay in ICU patients.[15,16]

On the other hand, the NUTRIC screening tool, validated by Heyland[17] and recommended by the American Society for Parenteral and Enteral Nutrition (ASPEN),[18] was specifically elaborated to identify nutritional risk in critically ill patients and may benefit from aggressive nutritional therapy. This tool classifies individuals according to the following criteria: (I) age, (II) Acute Physiology and Chronic Health Evaluation II (APACHE II) score, (III) Sequential Organ Failure Assessment (SOFA) score, (IV) comorbidities, (V) days of hospitalization before admission to the ICU, and (VI) interleukin-6 (IL-6). In 2015, a study conducted by Rahman et al. revalidated the tool excluding interleukin-6 (IL-6) since it is not a common biomarker.[6] This tool demonstrated that approximately 50% of patients admitted to the ICU have high nutritional risk.[19] A Brazilian study found similar results, in which the prevalence of high nutritional risk was observed in 46% of critically ill patients[20]. In addition, observational studies in critically ill patients have demonstrated that the high nutritional risk, identified by NUTRIC, is associated with unfavorable clinical outcomes and death.[15,19]

Even though NUTRIC was specifically designed for screening ICU patients[17], until the present moment there are no studies analyzing if such tool has a good performance when compared to NRS-2002 (reference method). Besides that, few studies have analyzed the association of high nutritional risk assessed by these tools, with clinical outcomes in critical patients. For these reasons, the objectives of this study are: (1) to assess nutritional risk through NRS-2002 and NUTRIC tools, (2) to identify NUTRIC performance when compared to

NRS-2002, and (3) to identify the possible associations of high nutritional risk, assessed by these tools, with the clinical outcomes of critically ill patients admitted into an ICU.

Materials and Methods

Patients

A prospective cohort study was performed with critically ill patients admitted to the ICU of Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, Brazil. The cohort included adult patients (age ≥ 18 years, of both genders, admitted in the period of October (2017) to January (2018). Patients with advanced terminal illness, neurodegenerative diseases, therapeutic limitations, and pregnant women were excluded from the research. The selection process is presented in **Figure 1**.

Patients were selected through daily screening in a maximum period of 72 hours after admittance to the ICU. They were accompanied until the hospital discharge or death. All data used in this research was taken from physical and electronic records, from patient, assistant staff, family and/or companions. No modifications in the patients' treatment were performed during the hospitalization period.

The study was conducted according to the guidelines of the Declaration of Helsinki and all procedures involving patients were approved by the Hospital Ethics Committee (protocol #170524). All patients or their legally responsible person signed an informed consent form.

General evaluation

Clinical e demographic characteristics as diagnosis, age, gender, and, ethnicity were collected from electronic records. Other outcome measures included body mass index (BMI), length of stay (LOS) in the hospital (days), length of stay in ICU (days), readmission in ICU, presence of infection during hospitalization (according to the medical records), and death. The following infectious complications were considered: urinary tract, respiratory tract,

gastrointestinal tract, surgical wounds, central nervous system and cutaneous infections. All outcomes were obtained from medical records of each participant.

Nutritional Screening

The nutritional screening was performed by a trained nutritionist using two tools - Nutritional Risk Screening - 2002 (NRS-2002)[12] (**Supplement 1**) and Nutrition Risk in the Critically Ill (NUTRIC)[6] (**Supplement 2**) in the period of up to 72 hours after admission to the ICU. NRS-2002 classified nutritional risk through the score sum considering nutritional status and disease severity. Patients older than 70 years old received an extra point to the screening. NUTRIC score was calculated based on patient's age, number of comorbidities, number of days at the hospital before ICU admission, *Acute Physiology and Chronic Health Evaluation II* (APACHE II)[21] score and *Sequential Organ Failure Assessment* (SOFA)[22] score. The SOFA score was obtained with platelet count, serum total bilirubin, serum creatinine, mean blood pressure, vasopressor use, arterial oxygen partial pressure /inspired oxygen fraction ratio (PaO2/FiO2). The APACHE II score was obtained through axillary temperature, mean blood pressure, heart rate, respiratory rate, arterial oxygen partial pressure, and serum levels of leukocytes, creatinine, potassium, sodium, and hematocrit, besides age and diagnosis.

Statistical Analyses

Data are presented as mean and standard deviation, median (25th – 75th), or number (%), and compared using t-Student, Mann-Whitney U and, $\chi 2$ tests, respectively. The nutritional risk was assessed by two nutritional risk screening tools: NRS-2002 and NUTRIC, and then classified per tools scores: score < 5 and ≥ 5 points. As a result, patients with a ≥ 5 score were considered at high nutritional risk. Multiple logistic regression analysis was used to calculate the odds ratio (OR) and their respective 95% CIs for to identify the association of the ICU LOS and clinical outcomes, adjusted for gender. ICU LOS was categorized according to the

cutoff point established in the literature (≥ 7 days).[25] The agreement between the screening tools was calculated through the *Kappa* coefficient. *Kappa* varies from 0-1: a value <0.2 indicates poor agreement; 0.2-0.4 fair agreement; 0.4-0.6 moderate agreement; 0.6-0.8 substantial agreement; and >0.8 almost perfect agreement. [23] The performance of the NUTRIC to predict nutrition risk, according to the NRS-2002 high nutritional risk, was analyzed by sensitivity, specificity, and area under the *Receiver Operating Characteristic* (ROC) curve.

The calculations were performed with the Statistical Package for The Social Sciences (SPSS) 23.0 (Chicago, IL) software, and *P*- values < 0.05 were considered statistically significant. .

Results

A total of 200 patients were included (59.4 ± 16.5 years old, 53.5% female). The selection process is shown in **Figure 1**.

The patients' general characteristics are described on **Table 1**. The patients were classified by clinical diagnosis (72.5%), surgical (26%), and trauma (1.5%). Clinical patients were those who had clinical diagnosis with no surgical management; surgical patients were those who had acute abdomen and/or in perioperative; and trauma patients those who had polytrauma by car accidents. The white ethnicity was referred in 53.5% and the mean of BMI was 27.1 ± 8.3 Kg/m². The patients presented a high APACHE II and SOFA score.

The median length of hospital stay was 15.0 days, in the ICU it was 4.0 days and readmission to the ICU was observed in 9.5% of the patients. Regarding clinical outcomes, 56% of patients required mechanical ventilation and, 20.5% renal replacement therapy. Around 50% of the patients presented infections during the hospitalization period. The following infections were considered: respiratory tract (28%), urinary tract (12.5%), blood

(14%), cutaneous (5%), surgical wound (9%), gastrointestinal (3%), and central nervous system (1%). Among the admitted ICU patients, 36% died.

Association of high nutritional risk, evaluated by nutritional screening tools, with length of hospitalization and clinical outcomes of critically ill patients are described in the **Table 2**. Patients at high nutritional risk (n = 110; 55%), assessed by NRS-2002, were associated with prolonged ICU stay (5.0 *vs.* 3.0 days; p = 0.050), mechanical ventilation use (65.5% *vs.* 44.4%; p <0.001), infection (32.5% *vs.* 17.5%, p = 0.004), and death (42.7% vs. 27.8%; p = 0.030) when compared with patients who presented nutritional risk < 5 points. The length of hospital stay and renal replacement therapy did not show a significant association at high nutritional risk by NRS-2002. Patients at high nutritional risk evaluated by NUTRIC (n = 73; 36.5%) presented association with the renal replacement therapy (64.4% *vs.* 51.2%; p=0.003) and death (54.8 *vs.* 25.2%; p<0.0001) when compared to the other patients. No association was observed with length of hospital and ICU stay and other clinical complications.

The association between ICU LOS (≥ 7 days) and clinical outcomes was evaluated in logistic regression analysis, adjusted for gender (**Table 3**). The high nutritional risk (score ≥ 5), assessed by NRS-2002, was associated with mechanical ventilation use (OR = 2.51; CI 95% 1.38-4.57; p = 0.002), and presence of infection (OR = 2.50; CI 95% 1.37 – 4.58; p = 0.003). The positive associations at high nutritional risk assessed by NUTRIC were also observed with the renal replacement therapy (OR = 2.76; CI 95% 1.20 – 6.36; p = 0.017) and death (OR = 2.55; CI 95% 1.28 – 5.06; p = 0.008). When we adjusted the analysis for age and APACHE II the results of these regression models did not change (data not shown).

A weak agreement was observed when evaluating both nutritional screening tools, NRS-2002 and NUTRIC (Kappa = 0.192, p<0.001). NUTRIC performance was analyzed by ROC curve using the NRS-2002 as reference tool (**Figure 2**). NUTRIC demonstrated a sensibility of

46.4% and specificity of 25.6% in relation to the NRS-2002. NUTRIC showed a satisfactory performance in identifying nutritional risk when compared to NRS-2002 (area on ROC curve 0.697; between 0.621-0.767).

Discussion

In the present study, the prevalence of high nutritional risk in critically ill patients was 55% and 36.5% by NRS-2002 and NUTRIC, respectively. An association between high nutritional risk assessed by NRS-2002 and clinical outcomes was also observed. Other studies that used such screening tools to identify nutritional risk in ICU patients corroborate our results. [15,16, 19, 20]

High nutritional risk in critically ill patients is associated with clinical complications, such as morbidity and mortality increase, infections occurrence, and prolonged hospital stay.[14-16,19] In this study, we evaluated the association between high nutritional risk (score ≥ 5), assessed by NRS-2002 and NUTRIC, and clinical outcomes during ICU and hospital length of stay. Patients at high nutritional risk, assessed by NRS-2002, showed a longer period of days at the ICU, need of mechanical ventilation, infections, and death when compared to patients with a < 5 score. Similar results were shown in observational studies with ICU patients, where high nutritional risk assessed by NRS-2002 was statistically significant when associated to death. [14-16]

When we evaluated the high nutritional risk by NUTRIC, a higher prevalence of renal replacement therapy and death was observed in critically ill patients at high nutritional risk when compared to the other patients. Previous studies that used NUTRIC as a nutritional screening instrument also observed an association of high nutritional risk (score ≥ 5 points) with longer hospitalization and clinical complications such as use of mechanical ventilation and death. [15, 19, 20]

In our study, we observed that patients at high nutritional risk had a higher prevalence of death when compared to patients with a score < 5, independently of the screening tool used. Besides, a positive association was observed in patients at high nutritional risk with clinical outcomes. Critically ill patients at high nutritional risk presented higher chance of use of mechanical ventilation (51%), infection (50%), renal replacement therapy (76%), and death (55%).

In clinical practice, screening and assessment tools are used to evaluate nutritional status.[24] However, only NRS-2002 and NUTRIC tools include severity of trauma and/or disease.[18] In the present study, a weak agreement between both instruments was observed. Nevertheless, ROC curve demonstrated a good NUTRIC performance (sensibility of 46.4% and specificity of 25.6%) in relation to NRS-2002. Despite NUTRIC being created specifically for critically ill patients and being a quick and practical assessment tool when patients are unable to communicate, this score presents some limitations to be considered. NUTRIC does not include traditional risk markers such as BMI, weight loss, food intake, or physical examination. Furthermore, there is a lack of criteria for the period of exposure to a high degree of severity of disease or trauma (metabolic stress). [25] Besides, it is possible that the use of such tool could be more complex in some ICUs, considering that some biochemical values, such as the interleukin-6 marker (IL-6), are not always available. In 2015, however, Rahman et al. revalidated this tool excluding the usage of the IL-6[6], which makes this instrument more applicable in the absence of this biomarker.

NRS-2002 was the first nutritional risk screening tool developed through medicine based in evidence.[12] NRS-2002 is efficient in identifying patients at high nutritional risk that may benefit from a precocious and aggressive nutritional support.[7,26] Indeed, in our study, NRS-2002 identified the prevalence of high nutritional risk in 55% of the critically ill patients

assessed. Moreover, we observed that patients at high nutritional risk showed a higher number of associations with clinical outcomes. It is possible that the screening factors used by this tool identify more specifically the nutritional risk. Some important point to consider about NRS-2002 is that all the ICU patients with an APACHE score of >10 are considered at nutritional risk, regardless of the nutritional variables. It has been suggested that the APACHE criteria >10 should be replaced by the expectancy of ICU permanence for, at least, a week (7 days), associated with the need of mechanical ventilation during the same period of time.[25]

Our study has some limitations. An analysis with a larger number of patients may provide more robust results. Also, this sample was composed by patients of a wide age range (including adults and elderlies) and with different diseases. We believe that assessing the nutritional risk according to the different diseases might be interesting and provide more accurate data for nutritional screening of ICU patients. Our sample included only patients that were admitted to the ICU, and our results cannot be extrapolated to all hospitalized patients. Indeed, there is still variability in the use of nutritional screening tools according to an American study conducted with hospitalized patients.[27] On the other hand, we emphasize that, until the present moment, there are no studies that demonstrate the performance of NUTRIC in relation to the NRS-2002 in screening of critically ill patients, and demonstrate the associations of high nutritional risk with the clinical outcomes during the period of ICU length of stay (5 days median). Perhaps some results may be more consistent in patients with longer ICU stay, as already suggested by Kondrup et al. [25]

Conclusion

Considering the results of this study in critically ill patients it is possible to conclude that the NUTRIC have a good performance in relation to NRS-2002 in identifying risk of malnutrition, and high nutritional risk is associated to higher risk of clinical outcomes,

including death (≥ 50%). In fact, the high nutritional risk assessed by NRS-2002 score was associated with a higher risk of mechanical ventilation (51%) and presence of infection (50%). On the other hand, the high nutritional risk, evaluated by NUTRIC score was associated with a higher risk of renal replacement therapy (76%) and death (55%). Regardless of which screening tool is used, we believe that the most important is identifying the nutritional risk as soon as possible (24-72 hours after the admission to the ICU).

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Conflict of interest

The authors declare that they have no competing interests.

Statement of Authorship

T. Steemburgo and A. Reis contributed to the conception and design of the study; T. Steemburgo, V. Luft, and J. Marchetti contributed to the analysis; J. Marchetti, A. Reis, and A. Forte contributed to data collection. T. Steemburgo, J. Marchetti, A. Reis, O. Franzosi and V. Luft contributed to drafting and review of the manuscript. All authors contributed to the interpretation of the results, critically revised the manuscript, gave final approval, and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Table 1. General Characteristics of Critically Ill Patients Admitted to the Intensive Care Unit (ICU) (n= 200).

	Descriptive statistics
Clinical and demographic data	
Diagnosis (clinical/surgical and trauma)	145 (72.5%)/52(26%)/3(1.5%)
Age (years)	59.4 ± 16.5
Gender (female)	93 (53.5%)
Ethnicity (white)	175 (87.5%)
BMI (kg/m²)	27.1 ± 8.3
APACHE II (score)	14.7 ± 4.1
SOFA (score)	5.0 (2.2 – 8.0)
Hospitalization and clinical outcomes	
Hospital LOS (days)	15.0 (8.0 – 24.5)
ICU LOS (days)	4.0 (2.0 – 8.0)
Readmission in ICU (yes)	19 (9.5%)
Use of mechanical ventilation (yes)	112 (56%)
Mechanical ventilation period (days)	3.0 (1.0 – 7.0)
RRT (yes)	41 (20.5%)
Period in RRT (days)	8.5 (3.0 – 15.7)
Infection (yes)	100 (50%)
Death (%)	62 (36%)

Body Mass Index, APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; LOS, length of stay; ICU, Intensive Care Unit; RRT, Renal Replacement Therapy.

Data are presented as number (%), mean ± standard deviation or median (25th - 75th).

Table 2. Stay Hospitalization and Outcomes Clinical of Critically Ill Patients Admitted to the Intensive Care Unit (ICU) According to High Nutritional Risk.

Stay hospitalization/ Outcomes clinical	Nutrition Screening Tools					
	NRS- 2002			NUTRIC		
	Score < 5 points (n = 90)	**Score ≥ 5 points*** (n = 110)	***P* Value**	**Score < 5 points** (n = 127)	**Score ≥ 5 points*** (n = 73)	***P* Value**
Hospital LOS (days)	14.5 (8.0- 4.2)	16.0 (8.0-25.0)	0.433	15.0 (6.0- 8.0)	14.0 (8.0-23.0)	0.700
ICU LOS (days)	3.0 (0.0-8.0)	5.0 (0.0-8.0)	**0.050**	4.0 (2.0-8.0)	5.0 (8.0-8.5)	0.180
Use of mechanical ventilation (yes)	40 (44.4%)	72 (65.5%)	**<0.001**	20 (15.7%)	31 (28.8%)	0.070
RRT (yes)	18 (20.0%)	23 (20.9%)	0.900	65 (51.2%)	47 (64.4%)	**0.030**
Infection (yes)	35 (17.5%)	65 (32.5%)	**0.004**	63 (31.5%)	37 (18.5%)	0.500
Death (yes)	25 (27.8%)	47 (42.7%)	**0.003**	32 (25.2%)	40 (54.8%)	**<0.001**

NRS-2002, Nutritional Risk Screening – 2002; NUTRIC, Nutrition Risk in the Critically; LOS, length of hospital stay; ICU, Intensive Care Unit; RRT, Renal Replacement Therapy.

Data are presented as mean ± standard deviation, median (25th - 75th) or number (%), and compared using t-Student, Mann-Whitney U and $\chi 2$tests, respectively.

Statistically significant *P*-values are shown in bold.

* Result considered as high nutritional risk.

Table 3. Risk of Length of Stay in the Intensive Care Unit and Clinical Outcomes for Critically Ill Patients at High Nutritional Risk.[a]

Nutrition Screening Tool	ICU LOS, OR (95% CI)	*P* value	MV, OR (95%CI)	*P* value	RRT, OR (95%CI)	*P* value	Infection, OR (95%CI)	*P* value	Death, OR (95%CI)	*P* value
NRS-2002 Score ≥ 5 points	1.32 (0.70-2.48)	0.394	2.51 (1.38 - 4.57)	**0.002**	1.11 (0.54-2.27)	0.780	2.50 (1.37-4.58)	**0.003**	1.56 (0.83- 2.93)	0.164
NUTRIC Score ≥ 5 points	1.75 (0.84- 3.65)	0.134	1.87 (0.95-3.67)	0.070	2.76 (1.20- 6.36)	**0.017**	1.29 (0.66-2.51)	0.455	2.55 (1.28-5.06)	**0.008**

OR, Odds Ratio; NRS-2002, Nutritional Risk Screening – 2002; NUTRIC, Nutrition Risk in the Critically; LOS, length of hospital stay; ICU, Intensive Care Unit; MV; Use of Mechanic Ventilation; RRT, Renal Replacement Therapy.

[a]All analyses were adjusted for gender.

Statistically significant *P*-values are shown in bold.

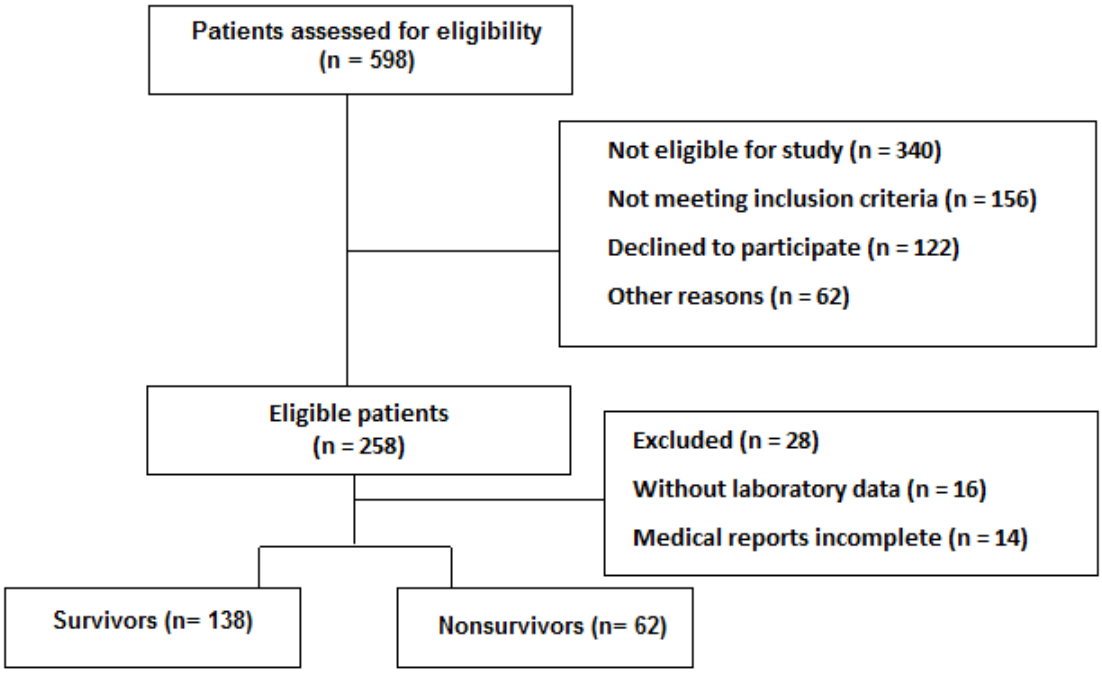

Figure 1. Flowchart of patient selection.

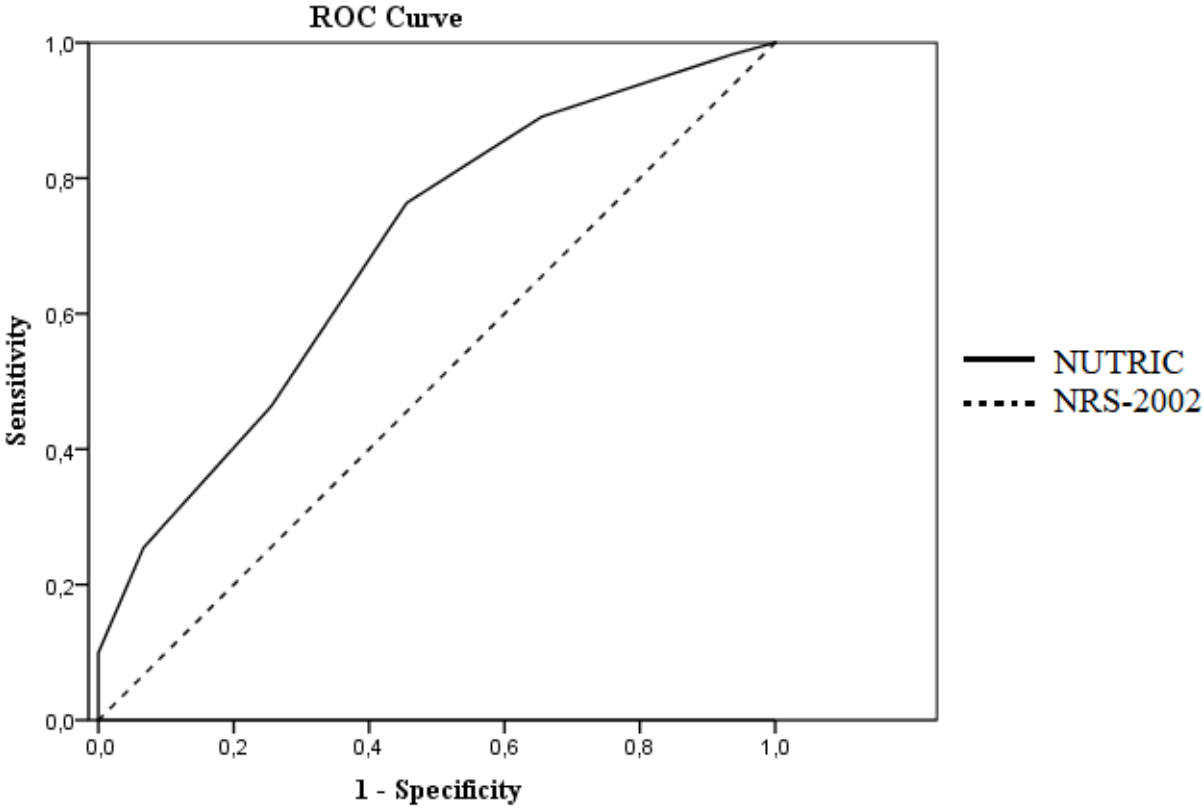

Figure 2. Receiver Operating Characteristic Curve (ROC) for the NUTRIC score calculated according to the NRS-2002 high nutritional risk (Score ≥ 5 points).

NRS-2002; Nutritional Risk Screening - 2002; NUTRIC; Nutrition Risk in the Critically Ill

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ANEXO A. NORMAS DE PUBLICAÇÃO DA REVISTA

Author Guidelines

***NCP* Author Guidelines**

General Information | Manuscript Categories | Manuscript Submission | Author Responsibilities |Academic Conduct | How to Prepare Your Manuscript | Submission Checklist

General Information

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Techniques and Procedures--Techniques and Procedures manuscripts are “how-to-do-it” contributions by practitioners. This section should include descriptions of certain procedures, treatments, or other aspects of managing patients receiving nutrition support. An unstructured abstract of ≤ 250 words is required.

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• Permission grants for previously published materials
• Additional requirements are outlined in the following table.

ANEXO B- NRS-2002

Avaliação do estado nutricional		Gravidade da doença	
Ausente Escore 0	Estado nutricional normal	Ausente Escore 0	Necessidades nutricionais normais
Leve Escore 1	Perda de peso >5% em 3 meses ou ingestão alimentar 50% a 75% do normal na semana anterior	Leve Escore 1	Fratura de colo de fêmur*; Pacientes crônicos notadamente com complicações agudas: cirrose*, DPOC*; *hemodiálise crônica diabetes e oncologia*
Moderado Escore 2	Perda de peso >5% em 2 meses ou IMC <18,5 + queda do estado geral ou ingestão 25% a 50% do normal na semana anterior	Moderada Escore 2	Grande cirurgia abdominal*; acidente vascular encefálico; *pneumonia grave; câncer hematológico*
Grave Escore 3	Perda de peso >5% em 1 mês (>15% em 3 meses) ou; IMC <18,5 + queda do estado geral ou ingestão 0% a 25% do normal na semana anterior	Grave Escore 3	Traumatismo de craniano*; transplante de medula óssea; pacientes em cuidados intensivos (APACHE>10)

Escore:_____ + Escore:___ Total:____

Idade: Se > 70 anos adicione 1 ao escore final = Escore total ajustado para idade

Fonte: Kondrup *et al.* (2003) [12]

ANEXO C – NUTRIC

Variável	Variação	Pontuação
Idade	<50	0
	50 - 74	1
	>75	2
APACHE	<15	0
	15 - 19	1
	20 - 27	2
	>27	3
SOFA	< 6	0
	6 - 9	1
	>9	2
Número de comorbidades	0 - 1	0
	> 1	1
Número de dias de internação prévios ao cuidado intensivo	0	0
	> 0	1
	Total:	

Fonte: Heyland *et al*. (2011) [17]