

Universidade Federal do Rio Grande do Sul
Hospital de Clínicas de Porto Alegre
Residência Multiprofissional em Saúde e em Área Profissional da Saúde
Programa de Atenção Cardiovascular

AMANDA FARIAS OSÓRIO

**VALOR PROGNÓSTICO DE FERRAMENTAS DE TRIAGEM E AVALIAÇÃO
NUTRICIONAL EM PACIENTES HOSPITALIZADOS COM INSUFICIÊNCIA
CARDÍACA: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE**

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Orientador: Profa. Dra. Gabriela Correa Souza

Coorientador: Dra. Gabriele Carra Forte

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Porto Alegre, 10 de janeiro de 2022.

A Comissão Examinadora, abaixo assinada, aprova o Trabalho de Conclusão de Residência “Valor prognóstico de ferramentas de triagem e avaliação nutricional em pacientes hospitalizados com insuficiência cardíaca: uma revisão sistemática e meta-análise”, elaborado por AMANDA FARIAS OSÓRIO, como requisito parcial para obtenção do título de nutricionista especialista em Atenção Cardiovascular.

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RESUMO

Introdução e objetivo: Estudos sugerem que a desnutrição é um fator prognóstico independente em pacientes com insuficiência cardíaca (IC). No entanto, ainda não existe um método padrão-ouro para avaliação e triagem nutricional nessa população, uma vez que a maioria das ferramentas vigentes sofre interferência das manifestações clínicas da doença, como edema e/ou inflamação. Diante disso, esta revisão sistemática e metanálise tem com objetivo avaliar o valor prognóstico de diferentes instrumentos de avaliação e triagem nutricional sob os parâmetros de reinternação e mortalidade em pacientes hospitalizados por IC. **Métodos:** A estratégia de busca foi aplicada à cinco bases de dados eletrônicas, com publicações até maio de 2021. Foram considerados elegíveis estudos com indivíduos com IC hospitalizados que avaliaram o estado e risco nutricional por meio de instrumentos de avaliação e triagem nutricional e sua associação com mortalidade e/ou reinternação. Os estudos foram agrupados de acordo com os diferentes desfechos clínicos e com o tipo de instrumento de triagem/avaliação nutricional utilizado. Os intervalos de confiança de 95% (IC95%) e a razão de risco (HR) entre os diferentes grupos foram calculados usando um modelo de efeitos aleatórios. Foi utilizado o método de variância inversa. **Resultados:** Dos 42 estudos incluídos, 36 avaliaram a mortalidade, 7 readmissão hospitalar e 9 o desfecho composto de eventos cardiovasculares. A maioria dos estudos mostrou que pior estado nutricional foi significativamente associado ao maior risco de mortalidade e/ou hospitalização. Na análise quantitativa (metanálise) dos instrumentos de triagem nutricional, o maior risco nutricional avaliado por quatro instrumentos (Controle do Estado Nutricional (CONUT), Índice de Risco Nutricional Geriátrico (GNRI), Triagem de Risco Nutricional (NRI), Índice Nutricional Prognóstico (PNI)) foi associado à mortalidade por todas as causas e, quando comparado às ferramentas PNI e GNRI, 'estado nutricional alterado' rastreado pelo CONUT demonstrou maior magnitude de associação com mortalidade por todas as causas (HR 2,79; IC 95% 1,81, 3,59). Além disso, maior risco de mortalidade foi observado em indivíduos com “desnutrição grave” rastreados pela ferramenta CONUT (HR 4,29; IC 95% 1,98, 9,28). Não foi realizada análise quantitativa com os demais instrumentos por falta de dados. **Conclusão:** Pior estado nutricional associou-se significativamente a maior risco de mortalidade e/ou hospitalização. Maior risco nutricional foi associado a pior prognóstico e maior mortalidade em pacientes com IC hospitalizados, principalmente quando rastreados pela ferramenta CONUT.

PALAVRAS-CHAVE: Insuficiência Cardíaca; Avaliação nutricional; Desnutrição

ABSTRACT

Background and aim: Several studies have suggested that malnutrition is an independent prognostic factor in patients with heart failure (HF). However, there is still no gold standard, universally accepted, methodology for nutritional assessment and screening in this population, since most instruments suffer interference from the disease manifestations, such as edema or inflammation. Therefore, we conducted a systematic review and meta-analysis in order to assess the role of different assessment and nutritional screening tools in the rehospitalization and mortality of patients hospitalized with HF. **Methods:** Major electronic databases were searched for articles published until May, 2021. Studies with hospitalized HF individuals that assessed the nutritional status through nutritional assessment and screening tools, and its association with mortality and/or rehospitalization were considered eligible. Studies were grouped according to the different clinical outcomes and to the type of nutritional screening/assessment tool used. The 95% confidence intervals (CI95%) and Hazard Ratio (HR) among the different groups were computed using a random-effects model. The inverse variance method was used. **Results:** Of the 42 studies included, 36 evaluated mortality, 7 hospital readmission and 9 the composite endpoint of cardiovascular events. Most studies showed that worse nutritional status was significantly associated with higher risk of mortality and/or hospitalization. In the quantitative analysis (meta-analysis) of nutritional screening tools, higher nutritional risk assessed by four tools (Controlling Nutritional Status (CONUT), Geriatric Nutritional Risk Index (GNRI), Nutritional Risk Screening (NRI), Prognostic Nutritional Index (PNI)) was associated with all-cause mortality, and when compared to the PNI and GNRI tools, 'impaired nutritional status' screened by CONUT demonstrated a greater magnitude of association with all-cause mortality (HR 2.79; 95%CI 1.81, 3.59). In addition, a higher risk of mortality was observed in 'severe malnutrition' individuals screened by CONUT tool (HR 4.29; 95%CI 1.98, 9.28). No quantitative analysis was performed with the other tools due to lack of data. **Conclusion:** Worse nutritional status was significantly associated with higher risk of mortality and/or hospitalization. Higher nutritional risk was associated with poor prognosis and higher mortality in hospitalized HF patients, especially when screened by CONUT score.

KEYWORDS: Heart Failure; Nutrition Assessment; Heart Disease.

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1. INTRODUÇÃO

A insuficiência cardíaca (IC) é uma das principais causas globais de morbimortalidade, o que a torna um importante desafio e problema de saúde pública a nível nacional e mundial (MCDONAGH; METRA; ADAMO; GARDNER *et al.*, 2021). Com os avanços obtidos na terapia cardiovascular nas últimas décadas, houve um aumento da expectativa de vida e da prevalência de IC na população idosa, que vêm atingindo estágios mais avançados da doença com maior frequência (PETERSEN; DANZMANN; BARTHOLOMAY; BODANESE *et al.*, 2021; TRUBY; ROGERS, 2020).

Sinais e sintomas frequentemente presentes na IC congestiva, como fadiga e dispnéia, reduzem a capacidade de realizar atividades diárias, o que contribui para uma menor mobilização e maior perda de massa muscular (WITTE; CLARK, 2007). Além disso, a ativação de vias neuro-hormonais e adrenérgicas favorecem um estado catabólico nesses pacientes, que junto de outros fatores presentes na doença como anorexia, disabsorção, hipóxia e incremento do trabalho respiratório, contribuem para o aumento do risco nutricional (RN) (BERKOWITZ; CROLL; LIKOFF, 1963). Ademais, comorbidades como doença renal crônica e fragilidade, comumente presentes na IC, também favorecem a piora do estado nutricional (EN) nessa população (ANKER; PONIKOWSKI; VARNEY; CHUA *et al.*, 1997; RAHMAN; JAFRY; JEEJEEBHOY; NAGPAL *et al.*, 2016).

Já está demonstrado na literatura que pacientes com IC apresentam alta prevalência de desnutrição. O EN alterado já mostrou-se como um preditor independente para pior prognóstico clínico (mortalidade, rehospitalização, tempo de internação, pior qualidade de vida) em pacientes com IC (BILGEN; CHEN; POGGI; WELLS *et al.*, 2020; BONILLA-PALOMAS; GÁMEZ-LÓPEZ; ANGUITA-SÁNCHEZ; CASTILLO-DOMÍNGUEZ *et al.*, 2011; KATANO; YANO; KOUZU; OHORI *et al.*, 2021; RAHMAN; JAFRY; JEEJEEBHOY; NAGPAL *et al.*, 2016). Ademais, não raramente a desnutrição também progride para caquexia cardíaca, uma condição de desnutrição calórico-protéica caracterizada por perda muscular e edema periférico, com reversibilidade mais complexa e prognóstico desfavorável (RAHMAN; JAFRY; JEEJEEBHOY; NAGPAL *et al.*, 2016).

Diante disso, torna-se fundamental detectar o RN e o EN em seus estágios iniciais para que estratégias adequadas possam ser implementadas a fim de prevenir ou postergar desfechos clínicos indesejados. No entanto, os marcadores clássicos de desnutrição, como índice de massa corporal (IMC), circunferência da panturrilha e albumina sérica não são parâmetros confiáveis na detecção de risco nutricional na IC quando usados isoladamente, uma vez que sofrem interferência de características fisiopatológicas da doença, como edema e inflamação (LIN; ZHANG; LIN; LI *et al.*, 2016). Portanto, parece ser importante que a avaliação do RN e EN leve em consideração um conjunto de fatores, incluindo parâmetros como ingestão energética e proteica, perda de peso, massa muscular e gordura subcutânea, edema e comprometimento do estado funcional do paciente.

Tendo isso em mente, diversos instrumentos de triagem e avaliação nutricional que consideram mais de um parâmetro foram desenvolvidos. Ferramentas de triagem como *Mini Nutritional Assessment Short Form* (MNA-SF) (KAISER; BAUER; RAMSCH; UTER *et al.*, 2009), *Controlling Nutritional Status* (CONUT) (IGNACIO DE ULÍBARRI; GONZÁLEZ-MADROÑO; DE VILLAR; GONZÁLEZ *et al.*, 2005), *Geriatric Nutritional Risk Index* (GNRI) (BOUILLANNE; MORINEAU; DUPONT; COULOMBEL *et al.*, 2005), *Nutritional Risk Index* (NRI) (AZIZ; JAVED; PRATAP; MUSAT *et al.*, 2011), *Prognostic Nutritional Index* (PNI) (BUZBY; MULLEN; MATTHEWS; HOBBS *et al.*, 1980) contribuem para a identificação rápida de sujeitos em RN e para determinar se uma avaliação nutricional detalhada é indicada, de acordo com a *European Society of Parenteral and Enteral Nutrition* (ESPEN) (CEDERHOLM; BARAZZONI; AUSTIN; BALLMER *et al.*, 2017) e *American Society for Parenteral and Enteral Nutrition* (ASPEN) (MUELLER; COMPHER; ELLEN; DIRECTORS, 2011). Enquanto as ferramentas de avaliação nutricional, como *Mini Nutritional Assessment* (MNA) (GUIGOZ; VELLAS; GARRY, 1996) e *Subjective Global Assessment* (SGA) (DETSKY; MCLAUGHLIN; BAKER; JOHNSTON *et al.*, 1987) contribuem para diagnosticar de forma abrangente problemas nutricionais, lançando mão de uma combinação de parâmetros: histórico médico, nutricional e de medicação; exame físico; medidas antropométricas e dados laboratoriais (MUELLER; COMPHER; ELLEN; DIRECTORS, 2011).

No entanto, devido aos diversos fatores de confusão impostos pela fisiopatologia da IC, até os dias atuais não existe uma ferramenta considerada padrão-ouro, universalmente aceita, para avaliar RN e EN nessa população. Sendo assim, o objetivo desta revisão sistemática e meta-análise foi avaliar o papel de diferentes instrumentos de

triagem e avaliação nutricional e sua associação com a reinternação e mortalidade de pacientes hospitalizados por IC.

2. REVISÃO DA LITERATURA

2.1. INSUFICIÊNCIA CARDÍACA

A IC é uma síndrome complexa, degenerativa, caracterizada por anormalidade estrutural e/ou funcional do músculo cardíaco, que resulta em alteração das pressões intramiocárdicas e/ou do débito cardíaco (MCDONAGH; METRA; ADAMO; GARDNER *et al.*, 2021), sendo considerada a via final comum da maioria das doenças cardiovasculares (VIRANI; ALONSO; BENJAMIN; BITTENCOURT *et al.*, 2020). Atualmente, sua prevalência é de 1-2% na população mundial adulta (MCDONAGH; METRA; ADAMO; GARDNER *et al.*, 2021), o que a torna um importante problema de saúde pública devido ao elevado custo para o sistema de saúde (SAVARESE; LUND, 2017), uma vez que cursa com frequentes internações hospitalares e alta taxa de morbimortalidade. O último relatório publicado pela *American Heart Association* (AHA) previu que a IC atingirá pelo menos 8 milhões de norte-americanos (≥ 18 anos) entre 2012 e 2030, o que representará cerca 2,97% dos habitantes dos Estados Unidos em 2030 (VIRANI; ALONSO; BENJAMIN; BITTENCOURT *et al.*, 2020).

Ademais, avanços no tratamento da IC têm sido associados a uma maior expectativa de vida na população idosa (PETERSEN; DANZMANN; BARTHOLOMAY; BODANESE *et al.*, 2021). Isto, junto às alterações metabólicas de efeito catabólico inerentes à progressão da IC, pode impactar no EN e aumentar o risco de desnutrição destes pacientes (VON HAEHLING; DOEHNER; ANKER, 2007).

2.2. INSUFICIÊNCIA CARDÍACA DESCOMPENSADA E DESNUTRIÇÃO

A IC descompensada caracteriza-se pela presença súbita de sinais e sintomas típicos de IC, como dispneia, fadiga e congestão, com necessidade de terapia urgente. Existem diversos fatores que levam à descompensação da IC, dentre eles arritmias,

infecções, adesão inadequada ao tratamento farmacológico e não-farmacológico e doença coronariana aguda (MCDONAGH; METRA; ADAMO; GARDNER *et al.*, 2021).

Em estudo publicado em 2013, foi observado que pacientes hospitalizados por IC apresentaram taxa de mortalidade em um ano de 17,4% comparado a 7,2%, em pacientes ambulatoriais com IC (MAGGIONI; ANKER; DAHLSTRÖM; FILIPPATOS *et al.*, 2013). No Brasil, cerca de 11% de pacientes admitidos por IC morrem durante a internação (FERNANDES; FERNANDES; MAZZA; KNIJNIK *et al.*, 2020). Ademais, segundo Desai *et al.*, episódios de descompensação e, conseqüentemente, hospitalização, resultam na progressão da doença (DESAI; STEVENSON, 2012). À medida que a IC progride, vias metabólicas catabólicas são ativadas (RAHMAN; JAFRY; JEEJEEBHOY; NAGPAL *et al.*, 2016). Diversos mecanismos como aumento do metabolismo basal, hipóxia, distúrbios hormonais (ANKER; CHUA; PONIKOWSKI; HARRINGTON *et al.*, 1997), anorexia secundária ao aumento da expressão de citocinas inflamatórias (ADAMO; ROCHA-RESENDE; PRABHU; MANN, 2020), disabsorção associada à congestão, apetite reduzido (ANDREAE; VAN DER WAL; VAN VELDHUISEN; YANG *et al.*, 2021), saciedade precoce e náusea que levam a ingestão alimentar insuficiente já foram descritos como potenciais agravantes do RN nessa população (BILGEN; CHEN; POGGI; WELLS *et al.*, 2020; GROSSNIKLAUS; O'BRIEN; CLARK; DUNBAR, 2008; KATANO; YANO; KOUZU; OHORI *et al.*, 2021). A fisiopatologia da desnutrição na IC, portanto, é multifatorial.

Embora há muito tempo seja claro que pacientes com IC apresentam risco aumentado para desnutrição e alta prevalência de EN alterado (LIN; ZHANG; LIN; LI *et al.*, 2016), identificar de forma correta e acurada este risco permanece um desafio até os dias atuais. Tal cenário reforça a importância da instituição de métodos adequados para identificação de pacientes em risco de desnutrição, ou desnutridos, a fim de iniciar uma estratégia nutricional adequada de maneira precoce para postergar ou evitar desfechos indesejados.

Usualmente, os principais fatores levados em consideração na triagem de risco nutricional de um paciente são peso e o IMC, ambos parâmetros afetados em pacientes com IC descompensada devido retenção de líquidos (RAHMAN; JAFRY; JEEJEEBHOY; NAGPAL *et al.*, 2016). Além disso, algumas ferramentas tradicionais de triagem também fazem uso de níveis séricos de albumina como marcador de EN, marcador que pode não refletir o EN real do paciente em um momento de agudização da

doença, devido ao estado inflamatório aumentado (RAHMAN; JAFRY; JEEJEEBHOY; NAGPAL *et al.*, 2016).

De acordo com a ASPEN, triagem de RN consiste em um processo de identificar pacientes que podem estar desnutridos ou em RN, para determinar se uma avaliação nutricional mais detalhada é necessária (TEITELBAUM; GUENTER; HOWELL; KOICHEVAR *et al.*, 2005). Este processo deve ser simples, fácil e rápido, devendo identificar o RN com a maior acurácia possível (CORREIA, 2018). Diante disso, diversas ferramentas de triagem nutricional (BOUILLANNE; MORINEAU; DUPONT; COULOMBEL *et al.*, 2005; BUZBY; MULLEN; MATTHEWS; HOBBS *et al.*, 1980; IGNACIO DE ULÍBARRI; GONZÁLEZ-MADROÑO; DE VILLAR; GONZÁLEZ *et al.*, 2005; KAISER; BAUER; RAMSCH; UTER *et al.*, 2009; KONDRUP; RASMUSSEN; HAMBERG; STANGA *et al.*, 2003) foram propostas ao longo dos anos e amplamente utilizadas na prática clínica hospitalar. No entanto, devido às limitações impostas pelas características fisiopatológicas da IC descompensada, sua acurácia na detecção do risco nutricional torna-se questionável.

Uma vez identificado o risco para desnutrição, torna-se prudente a avaliação nutricional completa deste paciente, que consiste em uma anamnese mais abrangente, a fim de estabelecer uma estratégia nutricional adequada, uma vez que o EN alterado está relacionado com pior prognóstico na IC (LIN; ZHANG; LIN; LI *et al.*, 2016). Uma das consequências desta alteração é o desenvolvimento do quadro de desnutrição, que consiste no desequilíbrio metabólico gerado pelo aumento da demanda e gasto energético associado a ingestão calórica insuficiente e prejuízos absorptivos.

Uma vez desnutrido, o paciente evolui com disfunções metabólicas que resultam em catabolismo proteico e perda de massa muscular, além de redução da síntese proteica secundária ao aumento do estado inflamatório (VEST; CHAN; DESWAL; GIVERTZ *et al.*, 2019). Com o passar do tempo, estas alterações resultam em redução da capacidade funcional (RAHMAN; JAFRY; JEEJEEBHOY; NAGPAL *et al.*, 2016), que pode ser evidenciada pela maior dificuldade de locomoção e menor resistência para realizar atividades diárias, como tomar banho, vestir-se e alimentar-se. O processo de desnutrição e redução de capacidade funcional acaba tornando-se um ciclo vicioso, onde o primeiro contribui para o avanço do segundo, e vice-versa, resultando em pior prognóstico clínico para esta população (RAHMAN; JAFRY; JEEJEEBHOY; NAGPAL *et al.*, 2016).

Diversos autores já descreveram a desnutrição como um preditor independente de mortalidade e desfechos desfavoráveis em pacientes com IC (AGGARWAL; KUMAR;

GREGORY; BLAIR *et al.*, 2013; BONILLA-PALOMAS; GÁMEZ-LÓPEZ; ANGUITA-SÁNCHEZ; CASTILLO-DOMÍNGUEZ *et al.*, 2011; KATANO; YANO; KOUZU; OHORI *et al.*, 2021), e apesar da alta prevalência da condição nessa população, o processo de avaliação nutricional ainda é um desafio.

Frente ao exposto, identificar formas adequadas de triagem e avaliação nutricional destes pacientes, a fim de prevenir e/ou recuperar o quadro de desnutrição, deve ser uma prioridade para a equipe de saúde que acompanha pacientes hospitalizados por IC (PONIKOWSKI; VOORS; ANKER; BUENO *et al.*, 2016; ROHDE, 2018).

2.3. FERRAMENTAS DE TRIAGEM NUTRICIONAL

MNA-SF

A MNA-SF é uma ferramenta de triagem nutricional baseada na MNA. É um método simples e rápido de identificar risco nutricional, sendo composta por 6 questões que avaliam os pacientes quanto a mobilidade, estresse psicológico, problemas neuropsicológicos, IMC, redução na ingestão de alimentos, percentual de perda de peso ou doença aguda ativa durante os três meses anteriores a sua aplicação (KAISER; BAUER; RAMSCH; UTER *et al.*, 2009).

A MNA-SF foi desenvolvida pela Nestlé e validada em diferentes contextos clínicos internacionalmente (GUIGOZ, 2006; KAISER; BAUER; RAMSCH; UTER *et al.*, 2009; VELLAS; GUIGOZ; GARRY; NOURHASHEMI *et al.*, 1999), apresentando boa correlação com morbidade e mortalidade. A pontuação desta ferramenta varia de 0 a 14 e é dividida em 3 categorias: estado nutricional normal, risco de desnutrição e desnutrição, correspondendo aos valores de 12-14, 8-11 e 0-7, respectivamente.

CONUT

O CONUT é uma ferramenta de triagem nutricional objetiva, baseada em três parâmetros laboratoriais simples: albumina sérica, colesterol total e contagem total de linfócitos. Foi originalmente proposta por um grupo espanhol, em 2005, (IGNACIO DE ULÍBARRI; GONZÁLEZ-MADROÑO; DE VILLAR; GONZÁLEZ *et al.*, 2005) como uma ferramenta de triagem para desnutrição em pacientes hospitalizados, e também tem sido aplicada em pacientes hospitalizados com IC. Por se tratar de uma ferramenta

composta por parâmetros de fácil coleta, seu uso no meio hospitalar torna-se simples e viável, o que explica sua ampla utilização nos estudos que avaliam RN em IC.

O intervalo das pontuações CONUT é de 0 a 12. A pontuação classifica quatro categorias de estado nutricional: 0-1 como estado nutricional normal, 2-4 como risco leve de desnutrição, 5-8 como risco moderado e 9-12 como risco grave.

NRI

O NRI é uma ferramenta de triagem nutricional simples e bem validada para identificar pacientes hospitalizados em risco de complicações relacionadas à nutrição (AZIZ; JAVED; PRATAP; MUSAT *et al.*, 2011). Esta ferramenta foi desenvolvida pelo grupo Veteran's Affairs Total Parenteral Nutrition, em 1991, para uso avaliação de eficácia da terapia nutricional parenteral perioperatória em pacientes cirúrgicos (GROUP, 1991). Sua fórmula deriva de concentrações séricas de albumina e razão entre peso atual e peso ideal, sendo calculada da seguinte forma:

$$\text{NRI} = 1,519 \times \text{albumina sérica (g/L)} + 0,417 \times [\text{peso atual/usual (kg)}] \times 100$$

A partir dos valores de NRI obtidos, se dão, usualmente, quatro classificações: 1) severo risco nutricional (<83,5), 2) moderado risco nutricional (83,5-97,5), 3) leve risco nutricional (97,5-100) e 4) sem risco nutricional (>100). Os valores de ponto de corte da NRI foram determinados de acordo com perdas percentuais de peso de 5%, 10% ou 20%. As normas de perda de peso de 5% e 10% já foram validadas pelas Diretrizes para Triagem Nutricional da ESPEN (KONDRUP; ALLISON; ELIA; VELLAS *et al.*, 2003).

GNRI

O GNRI é uma versão revisada do NRI, criada por um grupo francês, no ano de 2005, com base na necessidade de uma ferramenta de triagem que não dependesse do peso atual do paciente, uma vez que esta medida nem sempre era de fácil avaliação no contexto clínico (BOUILLANNE; MORINEAU; DUPONT; COULOMBEL *et al.*, 2005). Portanto, Bouillanne *et al.*, substituíram o peso atual/usual, presente no NRI, por peso ideal. Além disso, esta ferramenta é adaptada especificamente para população idosa.

Esta ferramenta baseia-se nos níveis séricos de albumina, peso corporal atual e peso corporal ideal, sendo uma ferramenta de rastreamento simples para predizer o risco

de morbimortalidade relacionada à nutrição. O GNRI avalia o estado nutricional usando a seguinte equação:

$$\text{GNRI} = [1.489 \times \text{albumina sérica (g/L)}] + [41,7 \times (\text{peso corporal/peso ideal}) (\text{kg})].$$

Peso corporal ideal = $22 \times$ quadrado da altura em metros.

Pacientes com valores de GNRI ≥ 98 são considerados com estado nutricional normal, enquanto aqueles com GNRI de 92-97 apresentam risco leve de desnutrição, aqueles com GNRI de 82-91 apresentam risco moderado e aqueles com GNRI < 82 apresentam risco grave.

PNI

O PNI é calculado a partir da concentração sérica de albumina e da contagem total de linfócitos, o que a caracteriza como uma ferramenta de triagem nutricional objetiva e simples (BUZBY; MULLEN; MATTHEWS; HOBBS *et al.*, 1980). A PNI avalia o estado nutricional usando a seguinte equação:

$$\text{PNI} = [10 \times \text{albumina sérica (g / dL)}] + 0,005 \times \text{contagem total de linfócitos (/mL)}].$$

Pontuações de PNI relativamente baixas indicam pior estado nutricional. Pacientes com PNI > 38 são considerados como sem risco nutricional, enquanto aqueles com PNI de 35–38 estão em risco moderado de desnutrição e aqueles com PNI < 35 estão em risco grave.

NRS-2002

A ferramenta *Nutritional Risk Screening 2002* (NRS-2002) (KONDRUP; RASMUSSEN; HAMBERG; STANGA *et al.*, 2003) foi desenvolvida em 1992, por um pesquisador dinamarquês, para triar RN em pacientes adultos e idosos no âmbito hospitalar. A ferramenta baseia-se em dois pilares: estado nutricional e severidade da doença.

O primeiro é avaliado pelo IMC, perda de peso recente ($\geq 5\%$ nos últimos 1, 2 ou 3 meses) e ingestão alimentar na semana anterior à internação. O segundo categoriza o paciente de acordo com o estresse metabólico proveniente da doença ou condição clínica. O risco é calculado pela soma do escore quanto ao estado nutricional, que varia de 0 a 3,

e do escore da severidade da doença, que também varia de 0 a 3. Pacientes com ≥ 70 anos somam um ponto adicional. O paciente pode ter um escore total de 0 a 7, e qualquer escore ≥ 3 indica risco nutricional. Este instrumento mostrou-se adequado para identificar o EN de pacientes hospitalizados, por razões clínicas ou cirúrgicas, e tem seu uso recomendado pela ESPEN (KONDRUP; ALLISON; ELIA; VELLAS *et al.*, 2003).

2.4. FERRAMENTAS DE AVALIAÇÃO NUTRICIONAL

MNA

A MNA foi inicialmente desenvolvida para detectar desnutrição em pacientes geriátricos, na Suíça, em 1996 (GUIGOZ; VELLAS; GARRY, 1996). Nos últimos anos, também foi usada em outras populações, incluindo pacientes com IC (BONILLA-PALOMAS; GÁMEZ-LÓPEZ; ANGUITA-SÁNCHEZ; CASTILLO-DOMÍNGUEZ *et al.*, 2011; SUZUKI; KIDA; SUZUKI; HARADA *et al.*, 2015; YOST; TATOOLE; BHAT, 2018). Esta ferramenta conta com quatro pilares: avaliação antropométrica, avaliação geral, avaliação dietética e auto-avaliação.

O primeiro conta com aferição de IMC, circunferência do braço (CB), circunferência da panturrilha (CP) e perda de peso nos 3 meses anteriores à aplicação. O segundo considera fatores como independência para realizar atividades diárias, polifarmácia, presença de estresse agudo ou trauma recentes, mobilidade, úlceras por pressão e problemas neuropsicológicos. O terceiro pilar avalia quantas refeições completas o paciente faz por dia, quantas porções de proteína, vegetais e frutas consome, se houve ou não redução da ingestão alimentar não intencional recente, ingestão de líquidos e habilidade de auto alimentação ou necessidade de auxílio. E por fim, a auto avaliação que consiste na percepção do próprio paciente quanto ao seu estado nutricional: se se percebe com algum problema nutricional e qual percepção do seu estado nutricional em comparação com outras pessoas de mesma faixa etária. O escore estratifica os pacientes em 3 grupos: desnutridos (< 17 pontos), em risco de desnutrição (17-23,5 pontos) e estado nutricional normal (≥ 24 pontos).

SGA

A SGA é uma ferramenta de avaliação nutricional amplamente utilizada em uma variedade de ambientes clínicos. Foi inicialmente validada em 59 pacientes cirúrgicos

consecutivos admitidos em um hospital terciário canadense (DETSKY; MCLAUGHLIN; BAKER; JOHNSTON *et al.*, 1987).

Esta classificação previu o tempo de internação e o desenvolvimento de complicações destes pacientes e foi considerada reproduzível quando realizada de forma independente por 2 médicos diferentes. Desde a sua descrição original, a SGA foi validada em diferentes estados de doença e condições clínicas, incluindo insuficiência renal crônica, câncer, geriatria, pacientes criticamente enfermos e pacientes de medicina geral hospitalizados.

A ferramenta inclui uma avaliação do histórico médico (perda de peso, alterações na ingestão alimentar, sintomas gastrointestinais, capacidade funcional) e um exame físico (perda de massa muscular determinada pela perda palpável de volume; perda de gordura subcutânea determinada pela circunferência do braço; edema periférico e ascite). Sua pontuação consiste em três estados: A, B ou C, com “A” refletindo o estado nutricional normal, “B” refletindo desnutrição leve a moderada e “C” desnutrição grave.

3. JUSTIFICATIVA

Atualmente, são utilizadas diversas ferramentas para avaliar tanto RN, como EN, em pacientes hospitalizados. Pacientes internados por IC, entretanto, apresentam particularidades fisiopatológicas, como congestão e inflamação, que podem interferir na acurácia das ferramentas atuais.

Uma vez identificado o valor prognóstico de cada ferramenta, podem-se estabelecer novos protocolos de triagem e avaliação nutricional nas instituições hospitalares ou entidades hospitalares, como no Hospital de Clínicas de Porto Alegre (HCPA), conferindo benefícios para os pacientes e melhora da prática clínica dos residentes e nutricionistas envolvidos com esta população.

Diante disso, justifica-se o presente estudo, baseando-se na importância de verificar a validade das ferramentas multidimensionais comumente utilizadas na prática clínica e seu valor de predição de risco para desfechos prognósticos desfavoráveis associados à desnutrição, como mortalidade por todas as causas, mortalidade cardiovascular e/ou readmissão hospitalar.

4. QUESTÃO DE PESQUISA

Ferramentas multidimensionais utilizadas para avaliar risco e estado nutricional estão associadas com maior risco de mortalidade e readmissão hospitalar em pacientes hospitalizados por IC?

5. OBJETIVOS

5.1. OBJETIVO GERAL

Avaliar o valor prognóstico das ferramentas multidimensionais atualmente utilizadas para avaliar risco e estado nutricional de pacientes hospitalizados por insuficiência cardíaca.

5.2. OBJETIVO ESPECÍFICO

Identificar a prevalência de risco de desnutrição e desnutrição em pacientes hospitalizados por IC através das diferentes ferramentas utilizadas na literatura

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7. ARTIGO ORIGINAL

**PROGNOSTIC VALUE OF NUTRITIONAL SCREENING AND
ASSESSMENT TOOLS IN HOSPITALIZED PATIENTS WITH HEART
FAILURE:
A SYSTEMATIC REVIEW AND META-ANALYSIS**

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ABSTRACT

Background and aim: Several studies have suggested that malnutrition is an independent prognostic factor in patients with heart failure (HF). However, there is still no gold standard, universally accepted, methodology for nutritional assessment and screening in this population, since most instruments suffer interference from the disease manifestations, such as edema or inflammation. Therefore, we conducted a systematic review and meta-analysis in order to assess the role of different assessment and nutritional screening tools in the rehospitalization and mortality of patients hospitalized with HF.

Methods: Major electronic databases were searched for articles published until May, 2021. Studies with hospitalized HF individuals that assessed the nutritional status through nutritional assessment and screening tools, and its association with mortality and/or rehospitalization were considered eligible. Studies were grouped according to the different clinical outcomes and to the type of nutritional screening/assessment tool used. The 95% confidence intervals (CI95%) and Hazard Ratio (HR) among the different groups were computed using a random-effects model. The inverse variance method was used. **Results:** Of the 42 studies included, 36 evaluated mortality, 7 hospital readmission and 9 the composite endpoint of cardiovascular events. Most studies showed that worse nutritional status was significantly associated with higher risk of mortality and/or hospitalization. In the quantitative analysis (meta-analysis) of nutritional screening tools, higher nutritional risk assessed by four tools (Controlling Nutritional Status (CONUT), Geriatric Nutritional Risk Index (GNRI), Nutritional Risk Screening (NRI), Prognostic Nutritional Index (PNI)) was associated with all-cause mortality, and when compared to the PNI and GNRI tools, 'impaired nutritional status' screened by CONUT demonstrated a greater magnitude of association with all-cause mortality (HR 2.79; 95%CI 1.81, 3.59). In addition, a higher risk of mortality was observed in 'severe malnutrition' individuals screened by CONUT tool (HR 4.29; 95%CI 1.98, 9.28). No quantitative analysis was performed with the other tools due to lack of data. **Conclusion:** Worse nutritional status was significantly associated with higher risk of mortality and/or hospitalization. Higher nutritional risk was associated with poor prognosis and higher mortality in hospitalized HF patients, especially when screened by CONUT score.

KEYWORDS: Heart Failure; Nutrition Assessment; Heart Disease.

INTRODUCTION

Heart failure (HF) is a leading cause of morbidity and mortality worldwide, being a major public health problem [1]. The prevalence of HF increases with age, and as a result of advances in medical therapy, patients are living longer and reaching end stage disease more frequently [2].

Fatigue and breathlessness, present conditions in congestive HF, decrease the patient's daily activity, which contributes to muscle bulk loss and to an even lower total daily energy expenditure [3]. Also, neurohormonal and adrenergic pathway activation promote a catabolic state, and other contributing factors such as anorexia, malabsorption (associated with gut edema), liver dysfunction and increased work of breathing are believed to increase nutritional risk in HF patients [4]. Comorbidities, such as renal insufficiency and frailty, commonly present in HF, also contribute to worsen nutritional status [5, 6].

Malnutrition is frequently encountered in patients with HF and it correlates with mortality, rehospitalization, increased length of stay and poor quality of life in either chronic or acute decompensated heart failure (ADHF), being an independent prognostic factor [5, 7, 8]. Not rarely, malnutrition also progresses to cardiac cachexia, a condition of caloric-protein malnutrition with muscle wasting and peripheral edema, with more complex reversibility and unfavorable prognosis as well [5].

Thus, it is crucial to detect nutritional risk and status in its early stages so adequate strategies can be implemented in order to prevent or postpone adverse clinical outcomes and improve prognosis. Nonetheless, classic malnutrition markers (ie. body mass index (BMI), calf-circumference, and serum albumin) are not reliable parameters for detecting nutritional risk in HF when used alone, as they are commonly affected by pathophysiological features of the disease, such as edema and inflammation [9]. Therefore, it appears to be important that nutritional assessment take into account more than one factor, including parameters such as energy intake, significative weight loss, muscle mass and subcutaneous fat, edema and impaired functional status.

Considering that, several nutritional screening and assessment tools which consider more than one parameter have been developed. Screening tools such as Mini Nutritional Assessment-Short Form (MNA-SF) [10], Controlling Nutritional Status (CONUT) [11], Geriatric Nutritional Risk Index (GNRI) [12], Nutritional Risk Screening (NRI), Prognostic Nutritional Index (PNI) [13] contribute to quickly identifying subjects at nutritional risk and to determine whether a detailed nutritional assessment is indicated,

according to ESPEN [14] and ASPEN [15]. While assessment tools, such as Mini Nutritional Assessment (MNA) [16] and Subjective Global Assessment (SGA) [17] contribute to comprehensively diagnose nutritional problems that uses a combination of the following: medical, nutrition and medication histories; physical examination; anthropometric measurements and laboratory data” [15].

However, because of the many confounding factors present in HF, there is still no universally accepted gold standard methodology for assessing nutritional risk and status in this population. Lin et al. [18], in systematic review and meta-analysis, showed that nutritional risk assessed by multidimensional tools is an independent prognostic factor in patients with HF, however did not assess if the clinical setting impact on this matter. Therefore, the aim of this systematic review and meta-analysis was to assess the role of different assessment and nutritional screening tools and its association with rehospitalization and mortality in hospitalized patients with HF.

METHODS

The protocol of this review was registered in PROSPERO on July 15, 2021, with accession number CRD42021256271.

Data Sources and Search Strategy

The search strategy was applied to five databases: Medline, Embase, Web of Science, Lilacs, and Scopus on May, 2021. The following key concepts were applied: HF and nutrition assessment. The research question of the current systematic review, constructed according to Participants, Exposure, Comparison, and Outcomes criteria (Box 1) was: “Are multidimensional tools used for nutritional assessment and screening associated with higher risk of mortality and/or rehospitalization in hospitalized patients with HF?”. Detailed search strategy can be found in Supplementary box 1. Citation searches from selected included papers were also undertaken. No restrictions were applied on language or publication date when applying the searches. The PRISMA checklist was used to direct the protocol of this review [19].

Box 1. Participants, exposure, comparison, and outcomes criteria for inclusion of studies.

Parameter	Criteria
Participants	Hospitalized patients with heart failure
Exposure	Malnutrition or Nutritional risk identified by multidimensional tool
Comparison	Normal nutritional status/ absence of nutritional risk identified by multidimensional tool
Outcomes	All-cause death, cardiovascular death, rehospitalization, composite endpoint of mortality and rehospitalization

Study selection

Two reviewers (AFO, ÉCTR) independently screened the title, abstract and full text of the selected studies which met the inclusion criteria for eligibility. When discordance occurred between the two reviewers, a third one (GCS) was required and consensus was established. To ensure the reliability of the studies, the following inclusion criteria were considered in the selection: a) Patients ≥ 18 years hospitalized with HF, b) Assessment of nutritional status with multidimensional tool (more than on isolated parameter/marker), c) Assessment of the following prognostic parameters: All-cause mortality, cardiovascular mortality and/or rehospitalization, d) Available full-text e) Prospective and retrospective observational cohort studies. Abstracts, case-reports, articles with full-text not available or articles that were in a language reviewers could not carry out a reliable translation were excluded.

The Mendeley[®] reference management software was used during the selection procedure. The characteristics and data of the included studies were recorded in a Microsoft Excel spreadsheet (Microsoft Office[®] 2016).

Data Extraction

The same two researchers (AFO, ÉCTR) independently extracted the data using standardized data extraction forms and the defined eligibility criteria. The following

information was extracted from each article: name of the first author, year of publication, journal of publication, study location and name, sample size, age at entry to the study, sex, length of follow-up, outcome, study design, main results, left ventricular ejection fraction (LVEF), nutritional assessment tool used, adjustment factors, risk estimate (hazard ratio [HR]) and study quality.

Study Quality and Credibility of Evidence Assessment

Research quality was assessed using the Ottawa-Newcastle Assessment Scale (ONS) [20]. The quality of the studies was evaluated by two independent reviewers (AFO, ÉCTR) and a third reviewer (GCS) was consulted in case of disagreements. The ONS judges studies on broad perspectives such as the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies respectively. The maximum total score on this scale is 9. “Good” defined as a total score of 7–9, “fair” was defined as a total score of 4–6 and “poor” was defined as a total score of <4.

Statistical Analysis

Studies were grouped according to the different clinical outcomes (i.e., all-cause mortality, cardiovascular mortality, and rehospitalization) and to the type of nutritional screening/assessment tool used (i.e., MNA, MNA-SF, GNRI, CONUT, PNI, NRI, SGA, NRS-2002). The 95% confidence intervals (95% CI) and HRs among the different groups were computed using a random-effects model. The inverse variance method was used. Obtaining the HRs directly from the original article was the preferred method. When not available, an attempt to contact the author was done. In case of impossibility, the study was excluded from the meta-analysis. HR are reported for each outcome, for each group and tool. R statistical software were used to conduct the meta-analysis when at least two studies tested the same nutritional screening tool, same nutritional risk category and reported the same outcome (therefore, only the all-cause mortality outcome was quantitatively evaluated (meta-analysis)). The cut-off point of one tool were arbitrarily chosen in different papers. Heterogeneity was assessed with the I^2 statistic, and low, medium and high heterogeneities were defined at 25, 50 and 75%, respectively [21]. The χ^2 test for heterogeneity was also done and we judged a p value less than 0.05 significant. In order to better investigate the heterogeneity, if possible (minimum three articles in the analysis), sensitivity analysis and/or subgroup analyzes were performed. In subgroup

analyses, we grouped studies according to age (age <70 years and age ≥70) and follow-up time (≤1 year and >1 year).

RESULTS

Databases search generated 1548 references, including 195 in PubMed, 142 in Web of Science, 555 in Scopus, 194 in Lilacs and 462 in Embase. After removing duplicates, 806 studies remained. After title and abstract selection, 130 studies were selected for full-text review. The two independent reviewers analyzed the remaining studies and came down to 42 articles. Whenever there was a discordance, the third reviewer established a consensus. A flowchart of the search and selection process is presented in Figure 1. Description of excluded studies is presented in Supplementary table 1. The characteristics of the included studies are summarized in Table 1. There were 28 retrospective and 14 prospective cohort studies.

Quality Assessment

Evaluation of the quality of the included articles is described in Supplementary Table 2. Most studies assessed were classified as “good” according to NOS.

Publication Bias

No statistical tests were performed to identify publication bias since visual assessment of the funnel plot and the statistical hypothesis tests are not usually performed when less than 10 studies compose the meta-analysis, due to the low power to detect eventual publication bias.

Nutritional screening and assessment in hospitalized patients with HF

The search presented various multidimensional nutritional screening and assessment tools for the evaluation of nutritional risk and status of hospitalized patients with HF (Table 1). Eight different tools were more frequently used: six for nutritional screening (MNA-SF, GNRI, PNI, NRS-2002, CONUT and NRI) and two for nutritional assessment (MNA and SGA). The most commonly used tool was GNRI [22-37] and CONUT [30-43] in 16 studies each, PNI was used in 11 studies [30-32, 34-36, 44-47], MNA [47-52] in six, and NRI [53-57] in five studies. The MNA-SF was applied in four [47, 58, 59] and SGA [52] and NRS-2002 [60] both in one study each.

Prognostic values of the nutritional screening and assessment tools

Of the 42 studies included, 36 evaluated mortality, 7 evaluated rehospitalization, and 9 evaluated composite endpoint of cardiovascular events.

Prognostic value of nutritional screening tools

Thirty-two studies showed that higher nutritional risk was significantly associated with higher risk of adverse events (all-cause mortality, cardiovascular mortality and/or rehospitalization), twenty-nine being related to higher risk of mortality.

Thirty-seven studies evaluated nutritional risk by using nutritional screening tools (GNRI, CONUT, PNI, NRI, MNA-SF, NRS-2002). MNA-SF was used in four studies and was an independent predictor of mortality in three of them [47, 58, 59, 61]. Most of the studies which assessed the prognostic value of GNRI [22, 24, 25, 27-29, 31, 32, 35-37, 62] observed that lower GNRI values were independent predictors of all-cause or cardiovascular mortality and/or rehospitalization due to HF exacerbation. Ishiwata et al. however, only found association of nutritional risk with cancer mortality, but not cardiovascular or all-cause mortality [23], while Hirose et al. [26], Seo et al. [63], Uemura et al. [33] and Sze et al. [34] failed to find any association of nutritional risk by GNRI and poor prognosis. Eleven studies [30-32, 34-36, 44-47] assessed PNI's prognostic value, and all of them found it to be a significant predictor of mortality and/or poor outcomes. The NRS-2002 was only used by Tevik et al. [60], and in its adjusted analysis, patients at nutritional risk had more than five-time higher odds to die before the three-year follow-up than those not at nutritional risk. Sixteen authors used the CONUT score to assess nutritional risk [30-33, 35-43, 62]. Of these, only two [34, 61] did not found statistical relevance to its prognostic value. Finally, NRI was calculated by five authors and all of them found it to be an independent predictor of mortality [53-57].

Eight studies focused on the relationship between nutritional risk and the composite endpoint of mortality and rehospitalization and all of them found risk of malnutrition to be related with poorer prognosis [24, 32, 33, 36, 37, 39, 53, 54]. Uemura et al. [33] found a significant association of CONUT scores, but not GNRI, with poorer prognosis.

Nutritional Screening Tools

MNA-SF

Four studies evaluated the prognostic value of MNA-SF [47, 58, 59, 61]. All of them had the same endpoint: all-cause mortality. In total, 1583 patients were screened. Three authors came to very similar results, despite of different follow-up periods. Katano et al.[58], in a follow up of 1.52 years (IQR 0.96-2.94), found that as nutritional status worsened, all-cause mortality increased. Martín-Sanchez found that malnutrition as identified by MNA-SF was an independent factor associated with 30-day mortality compared to normal nutritional status [59] and Yost et al. [64] showed that ‘malnourished’ and ‘at risk’ groups demonstrated increased mortality compared to ‘well-nourished’ group ($p < .0001$). The effect remained significant and increased when the author combined the categories ‘at risk’ and ‘malnourished’ and compared them to the reference ($p < 0.1$). Boixader et al. [61], however, failed to find association of risk of malnutrition as identified by MNA-SF and mortality. Quantitative analysis was not possible due to lack of data available and/or impossibility to contact the author [47, 59, 61].

CONUT

Sixteen studies used CONUT to assess nutritional risk, accounting for 6998 patients [30-43, 61, 62]. Five studies had medium age < 70 years [31, 36, 37, 42, 43], and most had a follow-up of 1 year or more. Nine studies found nutritional risk evaluated by CONUT to be an independent predictor of mortality [30, 31, 35, 38, 40-43, 62]. Five evaluated mortality and/or rehospitalization [32, 33, 36, 37, 39] and all of them found higher CONUT scores to be predictive worst outcomes. Only two studies did not find such results [34, 61].

In the meta-analysis, 6 studies evaluated CONUT prognostic value categorically (CONUT classification: nutritional risk, malnutrition and severe malnutrition) and 5 studies as a continuous variable (CONUT score). In the categorical analysis, ‘severe malnutrition’ was associated with all-cause mortality (HR 4.29; 95% confidence interval (95%CI) 1.98, 9.28). The category ‘nutritional risk’, however, was not associated with worse prognosis (HR 1.86; 95%CI 0.90, 3.83). When all categories were evaluated together, impaired nutritional status, according to CONUT, was associated with all-cause mortality (HR 2.79; 95%CI 1.81, 3.59) (Figure 2, A).

Because of the high heterogeneity (I^2 88%) observed, we conducted a sensitivity and subgroup analysis. When the article of Chien et al. [32], 2019 was removed from the analysis, the study that presented most dissonant characteristics among the others (longer follow-up time), the magnitude of the association increased for the ‘malnutrition risk’ subgroup (HR 2.64; 95%CI 1.14, 6.08) and in also in general analysis (HR 3.15 95%CI 2.21, 4.48), impacting importantly on heterogeneity (I^2 45%). When Shirakabe et al. [62] and Iwakami et al. [38] studies were removed, both with follow-up time < 12 months, magnitude of associations tended to fall, however heterogeneity remained high (I^2 83%). Another analysis was performed by removing Saito’s [43] article since it was the only one with quality classified as “fair” and mean age >70. The magnitude of association decreased in ‘severe risk’ group and the heterogeneity fell to I^2 77%. In subgroup analysis by time of follow-up in ‘severe malnutrition’ and ‘nutritional risk’, when only studies with a follow-up of ≤ 1 year were analyzed, the magnitude of association increased and heterogeneity dropped significantly (HR 5.98 95%CI 3.33, 10.76; I^2 0% and HR 2.64 95%CI 1.14, 6.08; I^2 53%, respectively).

When studies which presented CONUT score as a continuous variable were analyzed, a statistically significant association with all-cause mortality was shown (HR 1.37; 95%CI 1.23, 1.53) (Figure 2, B). Removing La Rovere’s [42] (younger age and different follow-up) study had no important impact in the analysis. In subgroup analysis by time of follow-up, the subgroup of studies with time of follow up ≤ 1 year had a higher magnitude of association with the outcome in relation to the subgroup of studies with follow-up time > 1 year (HR 1.53; 95%CI 1.35, 1.74; I^2 23% and HR 1.30; 95%CI 1.16, 1.45; I^2 86%).

A few studies were not included in the quantitative analysis due to lack of data [31, 33, 36, 37, 39, 41, 61].

PNI

Eleven studies evaluated nutritional status with PNI, analyzing 7942 patients [30-32, 34-36, 44-47, 62]. Only three studies had medium age of <70 years [31, 36, 46] and most of the studies had a follow-up longer than 1 year. Not one study did not show PNI score as not relevant for predicting mortality or poor cardiovascular prognosis. Nine studies had all-cause death as endpoint and all of them found low PNI values to be independent predictors of mortality in hospitalized patients with HF [30-32, 34, 44-47, 62]. One study [35] evaluated in-hospital mortality and showed the same trend, while

Narumi et al. [36] assessed nutritional risk with PNI and two other tools and risk of cardiovascular events, and low PNI values were also independently associated with poor outcomes.

In the meta-analysis, 3 studies evaluated PNI's prognostic value categorically. The association between all-cause mortality and 'malnutrition' and 'risk of malnutrition' groups were significant (HR 3.34; 95%CI 1.29, 8.59) and (HR 1.83 95%CI 1.87, 2.87), respectively (Figure 4). Both subgroup and general analysis presented high heterogeneity, therefore we conducted a sensitivity analysis. We removed Çinier's [46] study, which presented younger subjects and longer time of follow-up, and the association tended to decrease, but remained significant and heterogeneity fell from 95% to 79%.

The remaining studies were not included in the quantitative analysis due to impossibility of data comparability (i.e. risk category, adjusted analysis) [30-32, 34, 36, 44, 45, 47].

GNRI

Sixteen studies assessed nutritional risk with GNRI, accounting for 8067 patients [22-37]. Of these, only four studies had median age <70 years [26, 31, 36, 37]. Most studies had a follow-up of more than 1 year and all-cause death was the endpoint of twelve of them. Nine authors [22, 25, 27-29, 31, 32, 35] found GNRI to be an independent predictor of mortality, while four [26, 30, 33, 34] did not find these results. One study found it to be an independent predictor for cancer mortality [23].

In the meta-analysis, 4 studies evaluated GNRI prognostic value categorically. 'Malnutrition risk' was associated with increased all-cause mortality (HR 2.54; 95%CI 2.02, 3.21, $I^2 = 37\%$) (Figure 5). For sensitivity analysis, we removed Nakamura's [25] (older subjects) study and heterogeneity decreased importantly ($I^2 = 7\%$).

Four studies evaluated GNRI as a continuous variable, and its score was inversely associated with all-cause mortality (HR 0.93 95%CI 0.91, 0.96, $I^2 = 69\%$) (Figure 6). In order to explore the high heterogeneity present in the analysis, we removed Honda's [27] study (classified as fair quality and shorter follow-up) and it decreased to $I^2 = 48\%$. In subgroup analysis by time of follow-up, the subgroup of articles with time of follow up >1 year had a higher magnitude of association (HR 0.95; 95%CI 0.94, 0.97; $I^2 0\%$).

Rehospitalization in 90 days after discharge and nutritional risk by GNRI were assessed by Kitamura et al [24]. Readmission avoidance rate was significantly lower ($p<0.001$) in the group with GNRI score <92. Composite endpoints were also evaluated

by four studies, three of them found nutritional risk assessed by GNRI to be of good prognostic value [29, 36, 37], while one study did not find such result [33].

Some studies were not included in the quantitative analysis due to impossibility of data comparability (i.e. risk category, adjusted analysis, outcome) [23, 24, 26, 31-34, 36, 37].

NRI

Five studies evaluated nutritional risk with NRI, accounting for 7388 patients. All five studies had all-cause death as an endpoint, and two studies also analyzed rehospitalization risk and the composite endpoint of mortality and/or rehospitalization. NRI scores were associated with higher mortality risk in four studies [53, 55-57]. Cho et al. [53] found that low NRI values independently predicted 1-year mortality when adjusted to potential cofounders, however, failed to find relevance when it came to rehospitalization risk. Aziz et al [54] found NRI significant association between lower NRI scores and the composite endpoint of mortality and/or rehospitalization.

In the quantitative analysis, two studies were included in the analysis that assessed NRI's classification continuously, demonstrating that higher scores were associated with improved prognosis (HR 0.96 95%CI 0.94, 0.97, $I^2 = 0\%$) (Figure 3).

A few studies couldn't be included in the analysis due to impossibility of data comparability (i.e. risk category, reported different measure of association) [53, 54, 56].

NRS-2002

Tevik et al. [60] were the first to assess the prognostic value of NRS-2002 in hospitalized patients with HF. The endpoint was all-cause mortality and the follow-up was three years. One hundred and thirty-one patients were evaluated. The overall mortality rate was 52.6% and patients at nutritional risk (N =51) died more compared to patients not at nutritional risk (N=18) ($P < 0.001$). When adjusted, the nutritional risk was associated with increased mortality (HR 2.78; 95% CI 1.53, 5.03).

Prognostic value of nutritional assessment tools

Six studies [47-52] evaluated the association between nutritional status assessed by multidimensional assessment tools and undesirable outcomes. Four of them [50-52,

59] showed that worst nutritional status was significantly associated with poorer prognosis.

All studies evaluated nutritional status with MNA and one with both MNA and SGA. 'Malnutrition' or being at risk of malnutrition according to the full version of MNA was associated with increased mortality in three studies [47, 50, 51]. The only study which evaluated SGA showed that its classification was a predictor of mortality for the malnourished patients [52]. Suzuki et al. [48] failed to find significant association of the MNA isolated and poorer prognosis, only finding relevance to the MNA score associated with transthyretin levels.

One study [49] focused on the relationship between nutritional status and rehospitalization and other [48] with the composite endpoint of all-cause death and/or rehospitalization. Both studies failed to find an association between nutritional status and their respective outcomes.

Nutritional Assessment Tools

MNA

Six studies assessed clinical outcomes using MNA, totalizing 1073 patients. Four [47, 50-52] of them measured all-cause mortality alone, one [49] rehospitalization and all cause death, and the other [48] the composite endpoint of all-cause death and/or rehospitalization. Three studies observed 'malnutrition' identified by MNA as an independent predictor of mortality [47, 50, 51]. Guerra-Sanchez et al. [52], however, did not find such significance. Both studies that evaluated MNA and its prognostic value over rehospitalization and all cause-death or composite endpoint failed to find statistical relevance [48, 49]. Suzuki et al. [48] only found the association of MNA and transthyretin (TTR) to be independent predictors of mortality and/or readmission due to HF worsening; the MNA alone, however, did not reach such significance. Kaluzna-Olesky et al. [49] also failed to find difference in survival or readmission rates according to nutritional status.

SGA

There was only one study that evaluated SGA prognostic value in hospitalized patients with HF [52]. The study assessed 377 patients with median age of 75 years and the SGA classification was a predictor of mortality for the patients classified as malnourished (Log Rank 7.02; $p = 0.03$).

Nutritional risk prevalence among nutritional screening tools

The prevalence of nutritional risk ranged from 10.6% [61] to 92% [58] among the screening tools. These data were reported by 35 of the 42 eligible studies. The prevalence of nutritional risk was lower and higher when using the MNA-SF, ranging from 10.6% to 92% [58]. Among studies which used GNRI and CONUT, the prevalence ranged from 26.8% [31] to 69% [36], and 20.1% [31] to 73.1% [40], respectively. According to NRS-2002, the only study using the tool identified a prevalence of 57% of nutritional risk, and studies which used NRI or PNI varied from 36.2% [57] to 68% [53] and from 21% [31] to 66.59%, respectively. Details are displayed in table 2.

Malnutrition prevalence among nutritional assessment tools

The prevalence of malnutrition ranged from 7.4%, assessed by SGA [52], to 24.7%, assessed by MNA [47]. As for risk of malnutrition, SGA identified it in 41.9% of the population studies, while MNA identified the highest in 68%, in Aggarwal's study [51].

DISCUSSION

In this systematic review and meta-analysis, impaired nutritional status was associated with a worse prognosis and higher risk of mortality in hospitalized patients with HF, especially when assessed by CONUT score. These findings are consistent with a previous systematic review and meta-analysis that evaluated multidimensional nutritional screening and assessment tools and its prognostic value in HF patients [18]. Both reviews demonstrated that multidimensional tools have good predictive value for clinical outcomes, especially mortality. Lin et al [18], however, found GNRI and MNA to have the stronger association with death, while this study demonstrated CONUT to be the more predictive.

With regard to this finding, a systematic review and meta-analysis [65] evaluated the association between nutritional risk assessed by CONUT and all-cause mortality. More than five thousand patients with HF were analyzed. Malnutrition according to CONUT classification conferred a higher risk of all-cause mortality (RR 1.92; 95% CI 1.58, 2.34), in-hospital mortality (RR 1.78, 95% CI 1.29, 2.46) and long-term mortality (RR 2.01, 95%CI 1.58, 2.57) compared to subjects not at nutritional risk. Also, per point increase in CONUT score significantly increased in 16% the risk of all-cause mortality.

The fact that CONUT demonstrates good prognostic value, not only in this study, but in the others mentioned above, can be explained by the fact that its determining items encompass different aspects of malnutrition/nutritional risk in this population (such as protein metabolism, immunity and lipid metabolism) [38, 66].

Another recent meta-analysis [67] evaluated GNRI's prognostic value in 7659 elderly patients with HF. GNRI <92 was associated with increased risk of all-cause mortality (HR 1.59, 95%CI 1.37, 1.85) when compared to GNRI >92. The author found that the relationship between GNRI and HF might differ based on the subtype of HF, favoring its value in patients with CHF rather than AHF, and specially in HFpEF. This study also demonstrated that GNRI have good predictive value to both mortality and rehospitalization. However, most of the studies that used GNRI in this review analyzed patients with acutely decompensated HF (ADHF). This may explain why GNRI showed lower association with outcomes compared to CONUT. Other tools such as PNI, NRI and NRS-2002 were also associated with prognosis.

Due to a small number of studies which evaluated the prognostic value of nutritional screening and assessment tools and rehospitalization, quantitative analyses were unable. Therefore, in terms of this outcome, further confirmation is required.

Accounting for nutritional status, two nutritional assessment tools were analyzed: MNA and SGA. MNA was an independent predictor of mortality in three [47, 50, 51] out of six studies, and SGA in one out of one [52]. Quantitative analysis was not possible due to lack of data.

As for clinical outcomes, MNA showed fair predictive value in hospitalized HF patients. The MNA has been widely used in hospitalized patients in acute-care settings, as it combines anthropometric and dietary habits assessment [68]. Two studies which evaluated adults with advanced HF showed 'malnutrition' or 'risk of malnutrition' to be independent predictors of mortality.

Aggarwal et al. [51] found that almost 90% of their sample presented nutritional disturbances according to MNA. That may reflect the establishment of cardiac cachexia, once the patients were at end-stage disease, with mean LVEF of 19%. MNA, differently from SGA, is composed by more assertive questions, such as weight loss, skin ulcers, presence of polimedication, protein intake (sources and servings), fruit, vegetables and fluid intake, mode of feeding, perception of health status and others. These parameters combined probably provide a better perception of nutritional status. However, classification may suffer interference from the interviewer or the patient itself, once there

are many questions that rely on memory, which may be a factor of over or under estimation, especially in the elderly. SGA [17], on the other hand, is a shorter form. It is composed by very important items for nutritional assessment, such as reduced food intake, weight loss, presence of edema, ascites, injury factor and anorexia or other gastrointestinal symptoms. However, it is a tool that many times is difficult to apply because of its subjectivity. The classification depends on the interviewer's ability to recognize physical signs of malnutrition and also the patient's capacity to accurately report the answers.

With regard to prevalence of nutritional risk, this review demonstrates a wide range (from 10.6% [61] to 92% [58]) among the screening tools. In a recent meta-analysis, Lv et al. [69] evaluated the prevalence of malnutrition and its effects on all-cause mortality in patients with chronic HF (CHF). Malnutrition was present in 46% of the 12537 patients included in the analysis, and compared to well-nourished patients, malnutrition increased the risk of all-cause mortality in 1.15 times (HR 2.15, 95%CI 1.89, 2.45). As seen in the present review, Lv et al. [69] also found high heterogeneity and a wide range of prevalence of malnutrition. This can probably be explained by the different tool's characteristics and cut-off points, as well as the heterogeneous sample analyzed.

Differences in the subpopulations of HF patients may have an important impact in this factor, once patients with advanced HF are probably at higher nutritional risk than patients with recently diagnosed HF, for example. This hypothesis is confirmed by Narumi et al. [36], who indicated that nutritional status is associated with Nt-ProBNP levels, and therefore disease severity. Considering that, it is suggested that a tool for nutritional screening in hospitalized patients with HF include multiple dimensions of risk and factors associated with prognosis in this population, such as: serum albumin levels, at least one nutritional parameter (e.g., reduced food intake, recent weight loss or physical examination with evidence of muscle loss). Also, the inclusion of other parameters such as insulin resistance, estimated glomerular filtration rate (eGFR), appetite perception and frailty may too should be a part of the screening. These parameters are frequently present in this population, impact on nutritional risk and may have a good prognostic value if analyzed together.

Considering the evidence presented in this systematic review and meta-analysis, in spite of current nutritional screening and assessment tools having good predictive value, there's still a wide range of discrepancy in its sensibility and accuracy. Also, malnutrition is widely present in HF, and still current tools diverge extremely in

prevalence percentage. This matter reinforces the need of further definition of a gold standard tool to evaluate HF hospitalized patients, so awareness and diagnosis of malnutrition and nutritional risk become a clearer process. Early identification of impairment would enable sooner implementation of adequate strategies. Therefore, adverse clinical outcomes could be postponed or avoided. For that reason, future studies should focus on finding an ideal multidimensional nutritional assessment tool for this population, or at least, better definition of cut-off points for the existing tools.

Other aspects

Risk of bias was identified in 15 studies, although most of studies demonstrated to have good quality according to NOS. NOS, however, fails to elucidate how to evaluate and report the score, which may explain the different scores found for the same studies by different authors [18]. Also, the tool presents limitations related to population representativeness, as well as lack of definition of the most important control factor. Therefore, it is important to consider that differences between studies could possibly have influenced the result.

Study Limitations

This review presents a few limitations. First, studies used different cut-off points to classify nutritional risk, which causes inconsistency and may have affected quantitative analysis. Second, hospitalized patients with HF many times suffer with the presence of edema due to decompensation of disease. Healthcare professionals are often uncertain about how to correctly discount the edema weight. This could affect the result of tools that consider current weight as a parameter. Regarding this matter, many studies do not report how and if the correction of the weight was done. Also, different inclusion and exclusion criteria were used in the studies, and since we did not specify other inclusion criteria than being hospitalized with HF, different disease stages were included, as well as different ages and LVEF classes. Finally, some studies had small sample sizes and thus lower statistical power. Half of the studies presented in this review were classified as 'fair' quality, so the hypothesis that the lack of better methodological rigor might have affected the results cannot be ruled out.

Strengths

To our knowledge, this is the first systematic review and meta-analysis to assess the prognostic value of nutritional screening and assessment tools focusing specifically on hospitalized patients with HF. Since this population has particular characteristics due to disease decompensation, it is of high clinical relevance to explore potential methods that may predict important clinical outcomes, such as hospitalization and mortality. Moreover, sensitivity and subgroup analysis were performed after quantitative analysis, so the results presented tend to be reliable apart from its own limitations. Also, this review was conducted according to Cochrane protocols and used five large electronic databases. The search was not limited to specific languages or periods, which ensures a comprehensive search. Finally, considering its inevitable limitations, this review provides evidence of which screening tool is more adequate for the hospital clinical setting assessment in HF patients, which haven't been done before.

CONCLUSION

The findings presented above suggest that malnutrition and risk of malnutrition assessed by multidimensional nutritional screening and assessment tools have good predictive value for readmission and mortality in hospitalized patients with HF. Therefore, these tools must be implemented in hospital clinical settings protocols. However, future studies should focus on the development of a gold standard tool for this population, or at least the better definition of current cut-off points, so nutritional screening and assessment become a clearer process, adequate strategies are early implemented and undesirable outcomes are avoided.

Table 1. Characteristics and main results of the articles included in the systematic review.

Multidimensional Nutritional Assessment Tools								
Reference	Tool	Population	Age (mean/median)	Design	N	Outcome	Follow-up	Outcome
Yost et al., 2014	MNA, MNA-SF	Subjects ≥18 years old with advanced HF	-	Retrospective cohort	162	All-cause death	1000 days (total)	66 (40.7%) of the patients within the cohort died: 14 in the malnourished group, 49 in the at-risk group, and 3 in the well-nourished group. 'Malnutrition' and 'at-risk of malnutrition' groups showed increased mortality compared to 'well-nourished' group (P < .0001). No HR available
Kaluzna-Olestky et al., 2020	MNA (polish version)	Subjects ≥18 years hospitalized for stable or ADHF	58 years (55 ± 11 years).	Prospective cohort	120	All-cause death, all cause rehospitalization and rehospitalization due to CV disease	344 days (total)	19 (16%) patients died from all the causes and 25 (21%) were rehospitalized due to HF exacerbation. Non-survivors did not differ significantly from the survivors as to the nutritional status. No HR available
Bonilla-Palomas et al., 2011	MNA	Subjects hospitalized for ADHF	73±10.1	Prospective cohort	208	All-cause death	22.1 ±11.6 months (mean)	37.2% patients died (CV death: 29%). As a result of the progression of the HF, 38 patients died (43.7%), 16 sudden deaths (18.4%), 8 due to other cardiovascular problems (9.2%) and 25 from non-cardiovascular causes (28.7%). "Malnutrition" HR for increased mortality=3.75, 95%CI 1.75, 8.02
Suzuki et al., 2015	MNA	Subjects hospitalized for ADHF	71.1 ± 14.7	Prospective cohort	52	All-cause death and rehospitalization due to HF decompensation	10.1 months (total)	Group L (MNA + TTR) HR for increased all cause-death and rehospitalization = 4.35, 95%CI 1.26, 17.74; 'malnutrition' HR for poorer prognosis = 5.89; 95%CI 1.34, 40.30

Aggarwal et al., 2013	MNA	Subjects ≥ 18 years hospitalized for advanced AHF in evaluation for LVAD implantation or heart transplant	59.3 \pm 14.1	Retrospective cohort	154	All-cause death	-	52 patients died. Sudden death (n = 13), intracranial bleed (n = 7), ischemic stroke (n = 6), sepsis (n = 6), gastrointestinal bleed (n = 6), multisystem organ failure (n = 6), and unknown (n = 8). 'malnutrition and at risk' OR for increased mortality risk, adjusted = 7.9; 95%CI 1.01, 62.30
Guerra-Sanchez et al., 2015	SGA, MNA	Subjects hospitalized for ADHF	75 \pm 10	Prospective cohort	377	All-cause death	4 years for the first subjects, 1 year for the last	194 patients (51.5%) died. SGA was a predictor of mortality in malnourished patients (p=0.03), while MNA failed to find significance (p=0.513). HR values not available

Multidimensional Nutritional Screening Tools

Reference	Tool	Population	Age (mean/median)	Design	N	Outcome	Follow-up	Outcome
Katano et al., 2021	MNA-SF	Subjects aged ≥ 65 hospitalized for management of HF	78 (72,83)	Retrospective cohort	419	All-cause death	1.52 years (0.96-2.94)	110 patients (26%) died (51 patients from HF-related causes; 22 patients from infection; 12 patients from cancer). 'Malnutrition' HR for increased mortality adjusted = 6.04 95%CI 0.81, 44.91; 'At risk of malnutrition' HR for increased mortality adjusted = 3.99 95%CI 0.53, 29.88.
Boixader et al., 2016	CONUT, MNA-SF	Subjects hospitalized for ADHF	-	Prospective cohort	253	All-cause death	12 months (total)	54 patients (22,2%) died. 'Malnutrition' HR for increased mortality risk adjusted = 1.020 95%CI 0.903, 1.153
Martín-Sanchez et al., 2019	MNA-SF	Subjects ≥ 65 years old with AHF	85 \pm 6.0	Prospective cohort	749	All-cause death	30 days (total)	Sixty-six (8.8%) patients died within 30 days. "Risk of malnutrition" OR for increased mortality risk adjusted 3.14 95%CI 1.10, 9.02

Kinugasa et al., 2013	GNRI	Subjects hospitalized with HFpEF	77±11	Prospective cohort	152	All-cause death; Cardiovascular death	2.1 years (1.2,3.6) (median)	39 patients (70.9%) had cardiovascular cause death: HF death (n=22, 40.0%), vascular death (n=11, 20.0%), and sudden death (n=6, 10.9%). Sixteen patients (29.1%) had non-cardiovascular cause death: infectious disease (n=7, 12.7%), respiratory disease (n=3, 5.5%), gastrointestinal disease (n=2, 3.6%), and others (n=4, 7.3%). 'low-GNRI' HR for increased mortality risk=2.667; 95%CI 1.527, 4.651. Lower GNRI as a continuous variable was an independent predictor of all-cause mortality. 'Low-GNRI' and 'high-GNRI' HR for increased HF re-hospitalization risk = 0.962; 95%CI 0.517, 1.795
Kitamura et al., 2019	GNRI	Subjects ≥65 years hospitalized for the first time for HF	-	Retrospective cohort	169	Rehospitalization	90 days (total)	GNRI 90-day HR for increased readmission risk=0.96; 95%CI 0.93, 0.99
Hirose et al., 2020	GNRI	Subjects hospitalized for ADHF (HFReEF and HFpEF)	67.1 ± 14.3	Retrospective cohort	451	In-hospital mortality	-	14 patients died, 10 (10.4%) patients with GNRI < 92 and 4 (3.8%) in GNRI ≥ 92. 'GNRI <92' OR for increased mortality, not adjusted=2.94 95%CI 0.89, 9.70. Lost significance in multivariate analysis
Nakamura et al., 2019	GNRI	Subjects ≥80 years hospitalized for ADHF	87.2 ± 4.9 years	Retrospective cohort	213	All-cause death	540 days (total)	low GNRI' HR for increased mortality risk = 2.28; 95%CI 1.15, 4.49
Honda et al., 2016	GNRI	Subjects ≥65 years hospitalized for ADHF	79±7	Retrospective cohort	490	All-cause death, cardiovascular death	189 days (66, 421) (median)	clinical outcomes occurred in 55 of study patients (11%), including 34 patients (7%) with CV death. 'Low GNRI' HR for increased mortality risk adjusted=0.92 95%CI 0.88, 0.95

Nishi et al., 2019	GNRI	Subjects ≥ 65 years hospitalized with HFpEF	78.5 ± 7.2	Retrospective cohort	110	All-cause death, cardiovascular death	503.5 (328.0,790.0) (median)	24 deaths occurred. Of these, 14 patients (58.3%) had a cardiovascular death: HF death (n=7, 29.2%), sudden death (n=4, 16.7%), and death due to other reasons (n=3, 12.5%). Ten patients (41.7%) experienced non-cardiovascular-related (n = 8) or unknown (n = 2) deaths. low GNRI as a categorical variable were independent predictor of all-cause death HR= 3.075, 95%CI 1.244, 7.600
Minamisawa et al.,2019	GNRI	Subjects aged ≥ 50 years old with HFpEF	-	Retrospective cohort	1677	Composite endpoint (CV death, heart failure hospitalization, or resuscitated sudden death)	2.9 years (1.9, 4.2) (median)	494 patients had the primary outcome (all-cause death and readmission). 'moderate to severe risk of malnutrition' HR for increased primary outcome (1.34; 95%CI 1.02, 1.76), CV death (2.06; 95%CI 1.40, 3.03), all-cause death (1.79; 95%CI 1.33, 2.42), hospitalization for any reason (1.28; 95%CI 1.05, 1.57), and hospitalization for non-CV reasons (1.53; 95%CI 1.22, 1.92) adjusted
Ishiwata et al., 2020	TCBI, GNRI	Subjects ≥ 18 years hospitalized in ICU for ADHF	-	Retrospective cohort	417	All-cause death	2.4 years (total)	94 patients (23%) died. 57 (61%) died from cardiovascular causes, while 7 (7%) were cancer-related deaths. 'LogGNRI' HR for increased all cause death (0.03 95%CI 0.01, 0.15), cardiovascular death (0.09 95%CI 0.01, 0.66) and cancer death risk (0.01 95%CI 0.01, 0.1)
Cheng et al., 2017	PNI	Subjects (HRrEF and HFpEF) hospitalized for ADHF	75.8 ± 13.2	Retrospective cohort	1673	All-cause death and cardiovascular death	31.5 \pm 27.6 months (mean)	742 (44%) patients died. 'lower PNI' per 1 SD HR for increased cardiovascular death (0.76 95%CI 0.66, 0.87) and total mortality risk (0.79 95%CI 0.73, 0.87)

Candeloro et al., 2020	PNI	Elderly subjects hospitalized with ADHF	83.56±7.15	Prospective cohort	344	All-cause death	158 days (range 2 to 180 days)	75 subjects (21.8%) died of whom 28 (8.1%) died during hospitalization. 'lower PNI' HR for increased mortality risk adjusted = 0.93; 95%CI 0.89, 0.98.
Çinier et al., 2020	PNI	Subjects ≥18 years old with HRrEF and ICD	60.9±14.4	Retrospective cohort	1100	All-cause death	48 ± 35 months (mean)	16% of the patients died. PNI values were divided in quartiles. PNI HR for increased mortality risk adjusted in Q2 = 1.76 95%CI 0.92, 3.38, in Q3 1.88, 95%CI 0.99, 3.58 and in Q4 8.12, 95%CI 4.65,14.17.
Yost et al., 2017	PNI	Subjects hospitalized with advanced HF for LVAD implantation	-	Retrospective cohort	288	All-cause death	-	PNI < 30' HR for lower survival = 0.888; 95%CI 0.795, 0.993;
Nishi et al., 2017	CONUT	Subjects ≥ 20 years hospitalized with HF	71.7±13.6	Retrospective cohort	482	In-hospital mortality , cardiovascular death, non-cardiovascular death	-	14 patients died, of which 10 deaths (71.4%) were due to a cardiovascular origin (8 HF, 1 ventricular fibrillation due to myocardial ischemic attack, and 1 septic shock due to infective endocarditis), and 4 deaths (28.6%) were non-cardiovascular in origin (1 gastrointestinal bleeding, 1 sepsis due to gastrointestinal perforation, 1 pneumonia, and 1 bladder cancer). 'higher CONUT' scores were associated with increased in-hospital mortality p=0.019.
Nishi et al., 2017	CONUT	Subjects ≥20 years hospitalized for ADHF	71.7±13.6	Retrospective cohort	482	All-cause death, cardiac death	541.5 (– 354,786) days (median)	14 patients died, of which 10 deaths (71.4%) were due to a cardiovascular origin (8 HF, 1 ventricular fibrillation due to myocardial ischemic attack, and 1 septic shock due to infective endocarditis), and 4 deaths (28.6%)

									were non-cardiovascular in origin (1 gastrointestinal bleeding, 1 sepsis due to gastrointestinal perforation, 1 pneumonia, and 1 bladder cancer). CONUT score as a continuous variable HR for increased mortality risk adjusted 1.42 95%CI 1.044,1.249
Iwakami et al., 2016	CONUT	Subjects age ≥ 20 years old (HRrEF and HFpEF) hospitalized for ADHF	75 ± 12	Prospective cohort	635	All-cause death and cardiovascular death	324 (106,554) days (median)		The primary outcome occurred in 64 (10%) subjects. 'higher CONUT' score HR for increased mortality risk adjusted 1.26 95%CI 1.11, 1.42. CONUT score ≥ 6 had a 3.67-fold increase in the risk as compared with those with a CONUT score of 0–1. 'higher CONUT' score HR for increased CV death adjusted 1.24 95%CI 1.05, 1.47.
Saito et al., 2020	CONUT	Advanced heart failure subjects who underwent LVAD implantation	41.6 ± 11.3	Retrospective cohort	63	All-cause death	23.9 months (total)		9 patients (14.3%) died. 'CONUT score ≥ 5 ' HR for increased mortality risk adjusted = 7.56; 95%CI, 1.33, 150.
La Rovere et al., 2016	CONUT	Subjects hospitalized with HF	61.3 ± 11.0	Retrospective cohort	466	All-cause death	12 months (total)		The 12-month event rate was 7.7% (36 subjects). 'CONUT score' HR for increased mortality risk = 1.701 95%CI 1.363, 2.122
Takikawa et al., 2021	CONUT	Subjects hospitalized with ADHF	78.0 (70.0–86.0)	Retrospective cohort	253	All-cause death, Rehospitalization due to HF	12 months (total)		Events occurred in 26.5% (all-cause mortality 10.3% and rehospitalization due to HF 20.6%). 'Malnutrition' by CONUT score HR for increased 1-year event 1.36, 95% CI 1.05–1.75
Uribarri et al., 2018	NRI	Subjects ≥ 18 years old who required cf-LVAD therapy	-	Retrospective cohort	279	All-cause death	12 months (total)		Normal NRI per 1 unit HR for increased survival adjusted 0.961; 95%CI, 0.941, 0.981

Cho et al., 2018	NRI	Subjects hospitalized with ADHF	68.4±14.5	Prospective cohort	5265	All-cause death and rehospitalization	1 year (total)	lower NRI' HR for increased mortality risk 1.84, 95% CI 1.50, 2.27
Aziz et al., 2011	NRI	Subjects hospitalized for ADHF	-	Retrospective cohort	1110	All-cause death, rehospitalization, cardiac death	2.7±1.0 years (mean)	low NRI" HR for increased mortality risk and readmission =0.42; 95% CI 0.34-0.50. NRI score for increased composite endpoint of all cause mortality and readmission OR 3.1 95%CI 2.34, 4.22
Barge-Caballero et al., 2017	NRI	Subjects aged >18 old in postoperative heart transplantation	-	Retrospective cohort	574	All-cause death	1 year (total)	102 patients (17.8%) died. NRI HR per unit for increased mortality risk, adjusted, = 0.95; 95%CI 0.93, 0.98
Adejumo et al., 2015	NRI	Subjects hospitalized with advanced HF	54±13	Retrospective cohort	160	All-cause death	6 months (total)	30 patients (19%) died. NRI adjusted per 10 units HR 0.60 (95% CI 0.39 to 0.93, and NRI as a continuous variable adjusted HR 0.89, 95% CI 0.69 to 1.14
Shirakabe et al., 2017	PNI, CONUT	Subjects with severely ACFH hospitalized in ICU	76 (67,82)	Prospective cohort	458	All cause death	365 days (total)	low-PNI' and severe-CONUT categories HR for increased mortality risk 2.060, 95% CI 1.302–3.259 and 2.238, 95%CI 1.050, 4.772, respectively
Chien et al., 2019	PNI, CONUT, GNRI	Subjects >20 years old hospitalized for ADHFpEF	77.2 ± 12.6	Retrospective cohort	1120	All-cause death, HF rehospitalization and composite endpoint of mortality and rehospitalization	1255 (371,1354) days (median)	394 patients died (206 CV deaths, 188 non-CV deaths). 680 (60.7%) developed adverse events (mortality or HF re-hospitalization). 'higher PNI' [HR 0.97 (95%CI: 0.95, 0.99)], and 'higher GNRI' [HR 0.98 (95%CI: 0.97, 0.99)] adjusted were associated with lower mortality and 'higher CONUT score' adjusted [HR: 1.08 (95%CI 1.02, 1.13)] exhibited higher mortality
Uemura et al., 2020	GNRI, CONUT	Overweight/obese subjects	70 (57,79)	Retrospective cohort	170	All-cause death, cardiac death,	1096 days (805,1096)	29 patients (17.1%) died, including 6 in-hospital deaths. 51 patients (30%) required

		hospitalized with ADHF				Rehospitalization due to HF	days) (median)	rehospitalization. (dichotomized) and mortality risk, adjusted, HR 2.306 95% CI 1.162-4.580.	CONUT score
Sze et al., 2017	PNI, GNRI, CONUT	Subjects hospitalized for ADHF with a primary diagnosis of HF secondary to left ventricular systolic dysfunction	80 (72,86)	Retrospective cohort	265	All-cause death	598 days (319,807) (median)	113 subjects died. 'lower GNRI' and 'higher CONUT score' and 'lower PNI' HR for increased mortality risk not adjusted 1.04 95%CI 1.03, 1.06, HR 1.42 95%CI 1.32, 1.53 and HR 1.14 95%CI 1.12, 1.17, respectively. 'lower PNI' HR for increased mortality risk adjusted 1.08 95% CI 1.01-1.16.	
Alatas et al., 2020	PNI, GNRI, CONUT	Subjects ≥ 65 years hospitalized for ADHF	74.7 ± 11.8	Retrospective cohort	628	In-hospital mortality	-	80 (12.7%) of the subjects died. PNI < 41.2 HR 1.29 95% CI 1.13-1.46, GNRI < 92 HR 1.93 95%CI 1.15, 2.61 and CONUT > 5 HR 1.79 95%CI 1.04, 1.76, adjusted for in-hospital mortality risk.	
Horiuchi et al., 2017	GNRI, CONUT	Subjects with HF rEF who underwent right heart catheterization	66 ± 13	Retrospective cohort	139	All-cause death, cardiovascular death, HF hospitalization, and composite of death or HF hospitalization	12 months (total)	HR for composite endpoint of death or HF hospitalization not available	
Narumi et al., 2013	PNI, GNRI, CONUT	Subjects hospitalized for HF	69.6 ± 12.3	Prospective cohort	388	Cardiovascular death, rehospitalization	28.4 (11.8,51.8) months (median)	There were 130 events, including 33 deaths and 97 re-hospitalizations. CONUT score HR 40.9, 95% CI 10.8–154.8], PNI score HR 6.4, 95%CI 5.4, 25.1, and GNRI score HR 11.6, 95%CI 3.7,	

								10.0 were independently associated with cardiovascular events
Seo et al., 2019	PNI, GNRI, CONUT	Subjects hospitalized for ADHF	74±13	Prospective cohort	371	All-cause death	2.5±1.4 years (mean)	112 subjects died, 50 patients died of CV death. CONUT score, PNI and GNRI as continuous variables, not adjusted, for the prediction of all cause mortality, HR 1.3182 95%CI 1.2181, 1.4265, HR 0.8996 95%CI 0.8703, 0.9299 and HR 0.9520 95%CI 0.9348,0.9695, respectively
Yoshihisa et al., 2017	PNI, GNRI, CONUT	Subjects hospitalized for ADHF	66.5	Retrospective cohort	1307	All-cause death	1146 days (total)	PNI, GNRI and CONUT scores and mortality risk adjusted HR 1.178 95% CI 1.051, 1.321; HR 1.372 95%CI 1.210, 1.556 and HR 1.387 95%CI 1.100, 1.749, respectively
Tevik et al., 2016	NRS-2002	Subjects ≥18 years hospitalized with HF	78 (37,95)	Prospective cohort	131	All-cause death	36 months (total)	69 patients (52.6%) died. NRS-2002 HR for increased mortality 2.78; 95%CI 1.53, 5.03

Age expressed as mean±standard deviation or median (interquartile range). Follow-up time expressed as total follow-up time or mean±standard deviation or median (interquartile range). -: information not reported in the original article. 95%CI: 95% confidence interval; ADHF: Acute decompensated HF; AHF: Acute heart failure; AUC: Area under the ROC curve; BMI: Body mass index; CONUT: Controlling Nutritional Status; CV: Cardiovascular; GNRI: Geriatric nutritional risk index; HF: Heart failure; HFpEF: Heart failure with preserved ejection fraction; HFrEF: Heart failure with reduced ejection fraction ; HR: Hazard ratio; HT: Heart transplant; ICU: Intensive care unit; LVAD: Left ventricular assist device; LVEF: Left ventricular ejection fraction; MNA: Mini Nutritional Assessment; MNA-SF: Mini Nutritional Assessment Short Form; MST: Malnutrition Screening Tool; MUST: Malnutrition Universal Screening Tool; NRI: Nutritional Risk Index; NRS-2002: Nutritional Risk Screening; NYHA: New York Heart Association classification; OR: Odds ratio; PNI: Prognostic nutritional index; SD: Standard deviation; SGA: Subjective Global Assessment; TCBI: index triglycerides × total cholesterol × body weight index.

Table 2. Prevalence of nutritional disturbance in eligible studies

STUDY	TOOL	PREVALENCE
Katano et al.	MNA-SF	52% 'malnutrition'; 40% 'risk of malnutrition'
Martín-Sanchez et al.	MNA-SF	79.3% 'risk of malnutrition'
Boixader et al.	CONUT, MNA-SF	NUTRITIONAL DISTURBANCE: 62% in CONUT; 10.6% in MNA-SF
Yost et al.	MNA; MNA-SF	24.7% 'malnutrition'; 65.4% 'risk of malnutrition'
Suzuki et al.	MNA	23.1% 'malnutrition'; 51.9% 'risk of malnutrition'
Kaluzna-Olestky et al.	MNA	9% 'malnutrition'; 52% 'risk of malnutrition'
Aggarwal et al.	MNA	22% 'malnutrition'; 68% 'risk of malnutrition'
Bonilla-Palomas et al.	MNA	13% 'malnutrition'; 59.5% 'risk of malnutrition'
Guerra-Sanchez et al.	MNA, SGA	MNA: 17.5% 'malnutrition'; 38.2% 'risk of malnutrition' SGA: 7.4% 'malnutrition'; 41.9% 'risk of malnutrition'
Kinugasa et al.	GNRI	48% 'GNRI <92'
Ishiwata et al.	GNRI	-
Kitamura et al.	GNRI	-
Nakamura et al.	GNRI	50.7% 'GNRI <92'
Hirose et al.	GNRI	47.7% 'GNRI <92'
Honda et al.	GNRI	33.06% 'GNRI <92'
Nishi et al.	GNRI	44.5% 'GNRI <92'
Minamisawa et al.	GNRI	11% 'GNRI <92'; 25% 'GNRI 92-98'
Cheng et al.	PNI	33.3% 'PNI <39.3'; 33.29% 'PNI 39.3-44.8'
Candeloro et al.	PNI	54.9% 'PNI <34'; 45% 'PNI > 34'
Çinier et al.	PNI	-
Yost et al.	PNI	44% 'PNI <30'; 56% 'PNI >30'
Tevik et al.	NRS-2002	57% 'nutritional risk'
Iwakami et al.	CONUT	30.9% 'CONUT 4-5'; 13.5% 'CONUT >6'
Takikawa et al.	CONUT	30.4% 'CONUT 5-12'
Nishi et al.	CONUT	46.1% 'CONUT 2-4'; 23.9% 'CONUT 5-8'; 3.1% 'CONUT 9-12'
Nishi et al.	CONUT	46.1% 'CONUT 2-4'; 23.9% 'CONUT 5-8'; 3.1% 'CONUT 9-12'
La Rovere et al.	CONUT	34% 'CONUT 2-4'; 20% 'CONUT 5-8'; 7% 'CONUT 9-12'
Saito et al.	CONUT	38% 'CONUT 5-12'
Cho et al.	NRI	21.9% 'NRI <89'; 23.4% 'NRI 89-95'; 22.7% 'NRI 95-100'; 32.5% 'NRI >100'
Aziz et al.	NRI	15.13% 'NRI <83.5'; 19.18% 'NRI 83.5-97.5'; 5.6% 'NRI 97.5-100'; 60% 'NRI >100'
Barge-Caballero et al.	NRI	5% 'NRI <83.5'; 22% 'NRI 83.5-97.5'; 10% 'NRI 97.5-100'
Adejumo et al.	NRI	-
Uribarri et al.	NRI	5.4% 'NRI <83.5'; 21.5% 'NRI 83.5-97.5'; 9.3% 'NRI 97.5-100'
Seo et al.	GNRI, CONUT, PNI	-
Yoshihisa et al.	GNRI, CONUT, PNI	NUTRITIONAL DISTURBANCE: 21.1% in PNI; 26.8% in GNRI; 20.1% in CONUT
Chien et al.	GNRI, CONUT, PNI	-
Sze et al.	GNRI, CONUT, PNI	NUTRITIONAL DISTURBANCE: 42% in PNI; 46% in GNRI; 46% in CONUT
Alatas et al.	GNRI, CONUT, PNI	-
Narumi et al.	GNRI, CONUT, PNI	NUTRITIONAL DISTURBANCE: 60% in PNI; 69% in GNRI; 61% in CONUT
Horiuchi et al.	GNRI, CONUT	28.77% 'GNRI <95'; 43% 'CONUT >3'
Uemura et al.	GNRI, CONUT	NUTRITIONAL DISTURBANCE: 57.6% in GNRI; 66.5% in CONUT
Shirakabe et al.	CONUT, PNI	NUTRITIONAL DISTURBANCE: 27.7% in PNI; 72% in CONUT

-: information not reported in the original article. CONUT: Controlling Nutritional Status; GNRI: Geriatric nutritional risk index; MNA: Mini Nutritional Assessment; MNA-SF: Mini Nutritional Assessment Short Form; NRI: Nutritional Risk Index; NRS-2002: Nutritional Risk Screening; PNI: Prognostic nutritional index; SGA: Subjective Global Assessment;

Figura 1. Study Selection Process

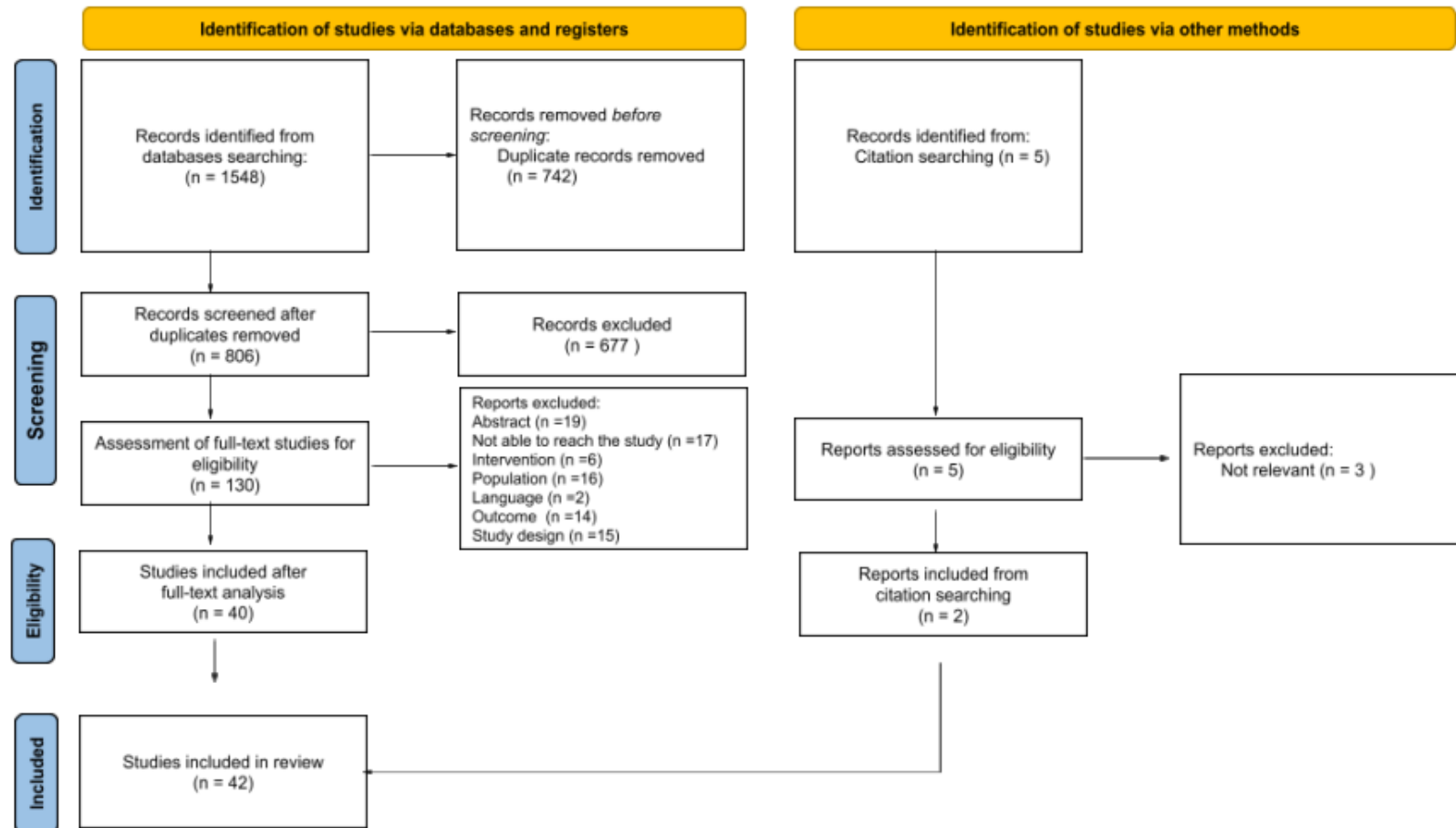


Figure 2. Association between all-cause mortality and nutritional screening assessed by the CONUT tool. A) CONUT score as a categorical variable; B) CONUT score as a continuous variable

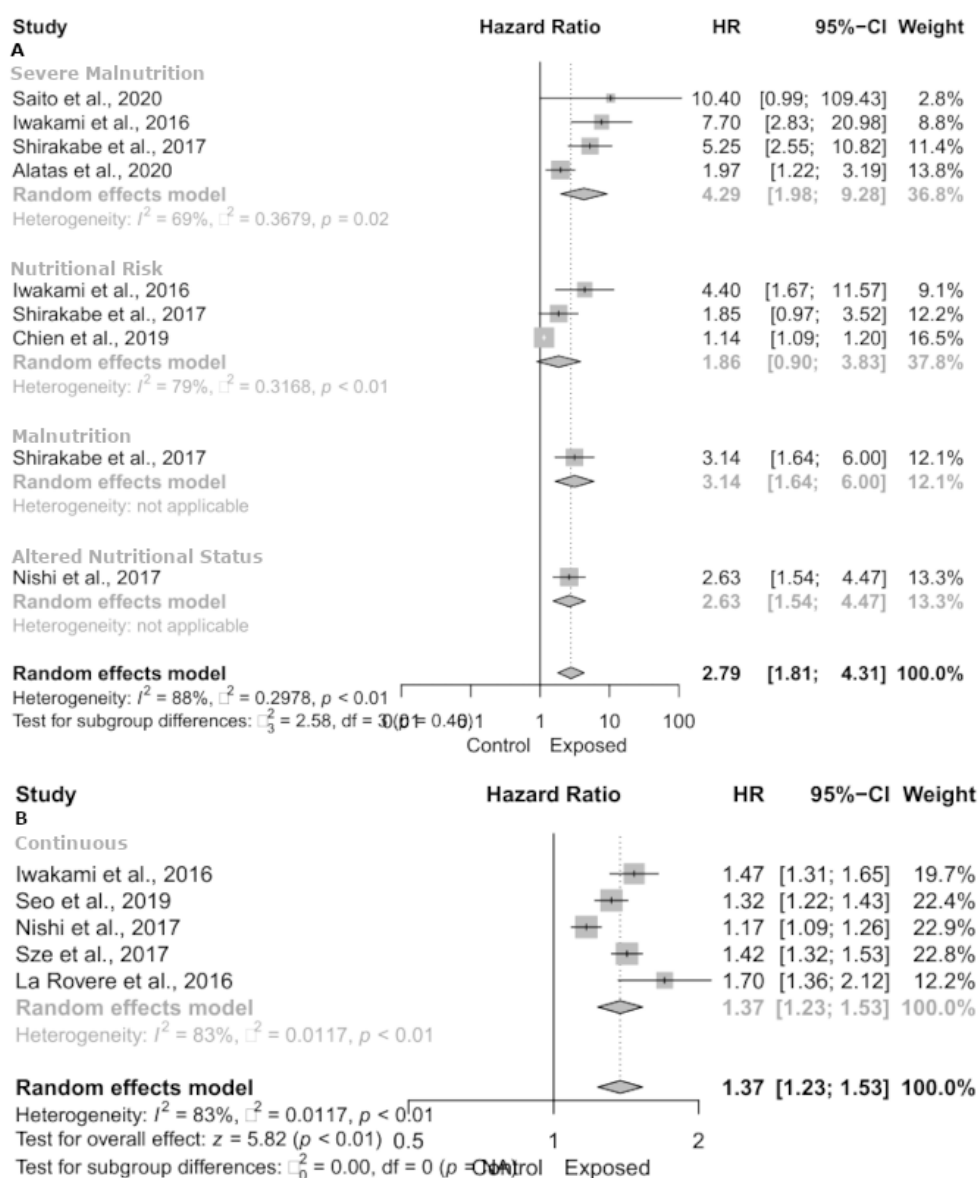


Figure 3. Association between all-cause mortality and nutritional screening assessed by the NRI tool

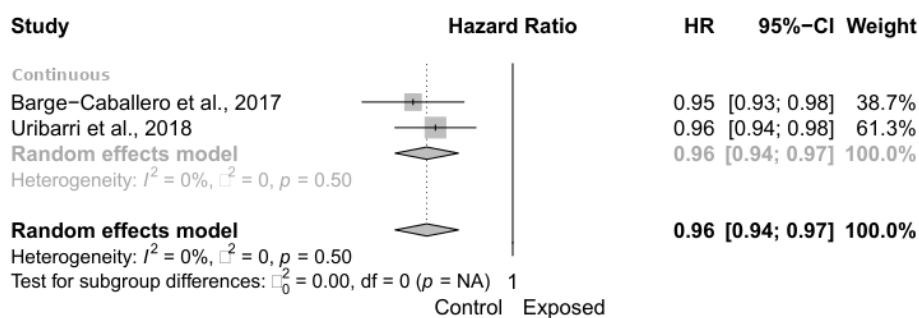


Figure 4. Association between all-cause mortality and nutritional screening assessed by the PNI tool. A) PNI as a categorical variable; B) PNI as a continuous variable

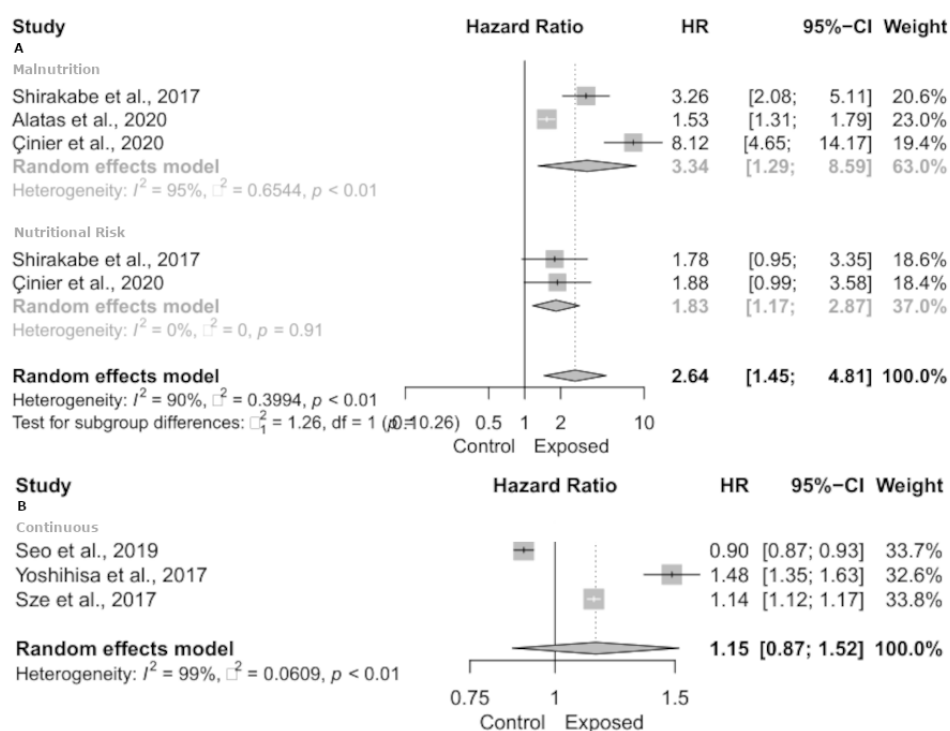
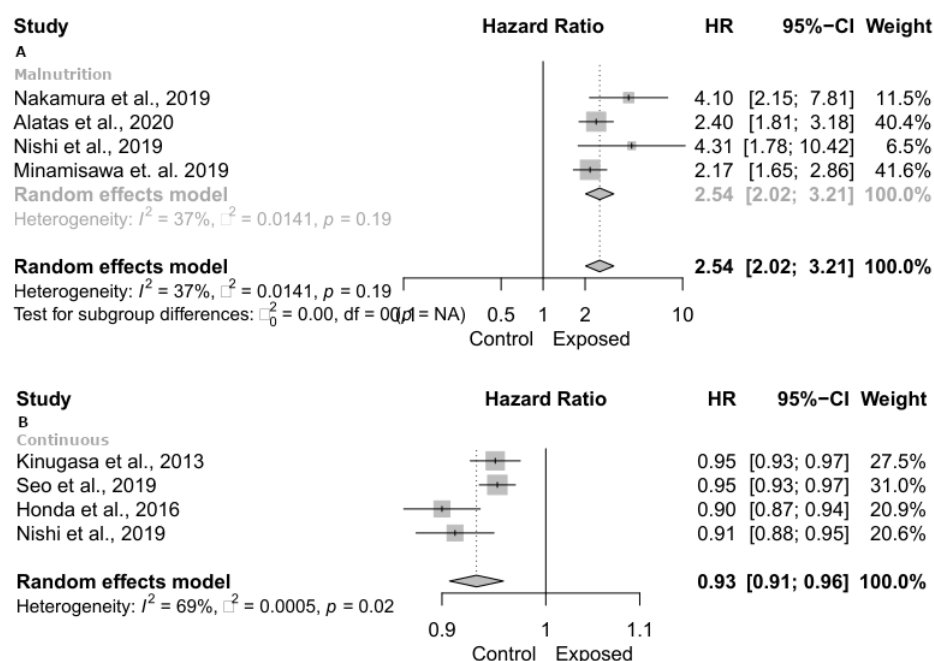


Figure 5. Association between all-cause mortality and nutritional screening assessed by the GNRI tool; A) GNRI as a categorical variable; B) GNRI as a continuous variable



Supplementary Box 1. Search Strategy

Database	Full Electronic Search Strategy
PubMed	<p>(((((((((((((Heart failure[MeSH Terms]) OR (Cardiac Failure[Title/Abstract])) OR (Heart Decompensation[Title/Abstract])) OR (Decompensation, Heart[Title/Abstract])) OR (Heart Failure, Right-Sided[Title/Abstract])) OR (Heart Failure, Right Sided[Title/Abstract])) OR (Right-Sided Heart Failure[Title/Abstract])) OR (Right Sided Heart Failure[Title/Abstract])) OR (Myocardial Failure[Title/Abstract])) OR (Congestive Heart Failure[Title/Abstract])) OR (Heart Failure, Congestive[Title/Abstract])) OR (Heart Failure, Left-Sided[Title/Abstract])) OR (Heart Failure, Left Sided[Title/Abstract])) OR (Left-Sided Heart Failure[Title/Abstract])) OR (Left Sided Heart Failure[Title/Abstract])) OR (HF[Title/Abstract])) OR (Ventricular Failure[Title/Abstract]) AND (((((((((((((((((((((((((((((((Nutrition Assessment[MeSH Terms]) OR (Assessments, Nutrition[Title/Abstract])) OR (Nutrition Assessments[Title/Abstract])) OR (Nutritional Assessment[Title/Abstract])) OR (Assessment, Nutritional[Title/Abstract])) OR (Assessments, Nutritional[Title/Abstract])) OR (Nutritional Assessments[Title/Abstract])) OR (Assessment, Nutrition[Title/Abstract])) OR (Nutrition Indexes[Title/Abstract])) OR (Indexes, Nutrition[Title/Abstract])) OR (Nutrition Indices[Title/Abstract])) OR (Nutritional Index[Title/Abstract])) OR (Index, Nutritional[Title/Abstract])) OR (Indices, Nutritional[Title/Abstract])) OR (Nutritional Indices[Title/Abstract])) OR (Nutrition Index[Title/Abstract])) OR (Index, Nutrition[Title/Abstract])) OR (Indices, Nutrition[Title/Abstract])) OR (Prognostic Nutritional Index (PNI)[Title/Abstract])) OR (Index, Prognostic Nutritional (PNI)[Title/Abstract])) OR (Indices, Prognostic Nutritional (PNI)[Title/Abstract])) OR (Nutritional Index, Prognostic (PNI)[Title/Abstract])) OR (Nutritional Indices, Prognostic (PNI)[Title/Abstract])) OR (Prognostic Nutritional Indices (PNI)[Title/Abstract])) OR (Prognostic Nutritional Index[Title/Abstract])) OR (Index, Prognostic Nutritional[Title/Abstract])) OR (Indices, Prognostic Nutritional[Title/Abstract])) OR (Nutritional Index, Prognostic[Title/Abstract])) OR (Nutritional Indices, Prognostic[Title/Abstract])) OR (Prognostic Nutritional Indices[Title/Abstract])) OR (Mini Nutritional Assessment[Title/Abstract])) OR (Assessment, Mini Nutritional[Title/Abstract])) OR (Assessments, Mini Nutritional[Title/Abstract])) OR (Mini Nutritional Assessments[Title/Abstract])) OR (Nutritional Assessment, Mini[Title/Abstract])) OR (Nutritional Assessments, Mini[Title/Abstract])) OR (Mini Nutrition Assessment[Title/Abstract])) OR (Assessment, Mini Nutrition[Title/Abstract])) OR (Assessments, Mini Nutrition[Title/Abstract])) OR (Mini Nutrition Assessments[Title/Abstract])) OR (Nutrition Assessment, Mini[Title/Abstract])) OR (Nutrition Assessments, Mini[Title/Abstract]))</p>
Embase	<p>'nutritional assessment'/de OR 'dietary assessment':ab,ti OR 'dietary evaluation':ab,ti OR 'nutrition assessment':ab,ti OR 'nutritional evaluation':ab,ti AND 'heart failure'/de OR 'backward failure, heart':ab,ti OR 'cardiac backward failure':ab,ti OR 'cardiac decompensation':ab,ti OR 'cardiac failure':ab,ti OR 'cardiac incompetence':ab,ti OR 'cardiac insufficiency':ab,ti OR 'cardiac stand still':ab,ti OR 'cardial decompensation':ab,ti OR 'cardial insufficiency':ab,ti OR 'chronic heart failure':ab,ti OR 'chronic heart insufficiency':ab,ti OR 'decompensatio cordis':ab,ti OR 'decompensation, heart':ab,ti OR 'heart backward failure':ab,ti OR 'heart decompensation':ab,ti OR 'heart incompetence':ab,ti OR 'heart insufficiency':ab,ti OR 'insufficiencia cordis':ab,ti OR 'myocardial failure':ab,ti OR 'myocardial insufficiency':ab,ti OR 'hf':ab,ti OR 'ventricular failure':ab,ti</p>
Scopus	<p>TITLE-ABS-KEY ("heart failure") OR TITLE-ABS-KEY ("Cardiac Failure") OR TITLE-ABS-KEY ("Heart Decompensation") OR TITLE-ABS-KEY ("Decompensation, Heart") OR TITLE-ABS-KEY ("Heart Failure, Right-Sided") OR TITLE-ABS-KEY ("Right-Sided Heart Failure") OR TITLE-ABS-KEY ("Myocardial Failure") OR TITLE-ABS-KEY ("Congestive Heart Failure") OR TITLE-ABS-KEY ("Heart Failure, Congestive") OR TITLE-ABS-KEY ("Heart Failure, Left-Sided") OR TITLE-ABS-KEY ("Left-Sided Heart Failure") OR TITLE-ABS-KEY ("HF") OR TITLE-ABS-KEY ("ventricular failure") AND TITLE-ABS-KEY ("Assessments, Nutrition") OR TITLE-ABS-KEY ("Nutrition Assessments") OR TITLE-ABS-KEY ("Nutritional Assessment") OR TITLE-ABS-KEY ("Assessment, Nutritional") OR TITLE-ABS-KEY ("Assessments, Nutritional") OR TITLE-ABS-KEY ("Nutritional Assessments") OR TITLE-ABS-KEY ("Assessment, Nutrition") OR TITLE-ABS-KEY ("Nutrition Indexes") OR TITLE-ABS-KEY ("Indexes, Nutrition") OR TITLE-ABS-KEY ("Nutrition Indices") OR TITLE-ABS-KEY ("Nutritional Index") OR TITLE-ABS-KEY ("Index, Nutritional") OR TITLE-ABS-KEY ("Indices, Nutritional") OR "Nutritional Indices" OR "Nutrition Index" OR "Index, Nutrition" OR "Indices, Nutrition" OR TITLE-ABS-KEY ("Prognostic Nutritional Index") OR TITLE-ABS-KEY ("Index, Prognostic Nutritional") OR TITLE-ABS-KEY ("Indices, Prognostic Nutritional") OR TITLE-ABS-KEY ("Nutritional Index, Prognostic") OR TITLE-ABS-KEY ("Nutritional Indices, Prognostic") OR TITLE-ABS-KEY ("Prognostic Nutritional Indices") OR TITLE-ABS-KEY ("Mini Nutritional Assessment") OR TITLE-ABS-KEY ("Assessment, Mini Nutritional") OR TITLE-ABS-KEY ("Assessments, Mini Nutritional") OR TITLE-ABS-KEY ("Mini Nutritional Assessments") OR TITLE-ABS-KEY ("Nutritional Assessment, Mini") OR TITLE-ABS-KEY ("Nutritional Assessments, Mini") OR TITLE-ABS-KEY ("Mini Nutrition Assessment") OR TITLE-ABS-KEY ("Assessment, Mini Nutrition") OR TITLE-ABS-KEY ("Assessments, Mini Nutrition") OR TITLE-ABS-KEY ("Mini Nutrition Assessments") OR TITLE-ABS-KEY ("Nutrition Assessment, Mini") OR TITLE-ABS-KEY ("Nutrition Assessments, Mini")</p>
Lilacs	<p>Heart Failure OR Cardiac Failure OR Congestive Heart Failure OR Heart Decompensation OR Heart Failure, Congestive OR Heart Failure, Left-Sided OR Heart Failure, Right-Sided OR Left-Sided Heart Failure OR Myocardial Failure OR Right-Sided Heart Failure AND Nutrition Assessment OR Índice Nutricional Prognóstico (INP)</p>
Web Of Science	<p>TI=("heart failure" OR "Cardiac Failure" OR "Heart Decompensation" OR "Decompensation, Heart" OR "Heart Failure, Right-Sided" OR "Right-Sided Heart Failure" OR "Myocardial Failure" OR "Congestive Heart Failure" OR "Heart Failure, Congestive" OR "Heart Failure, Left-Sided" OR "Left-Sided Heart Failure" OR "HF" OR "ventricular failure") Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos AND TI=("Nutrition Assessment" OR "Assessments, Nutrition" OR "Nutrition Assessments" OR "Nutritional Assessment" OR "Assessment, Nutritional" OR "Assessments, Nutritional" OR "Nutritional Assessments" OR "Assessment, Nutrition" OR "Nutrition Indexes" OR "Indexes, Nutrition" OR "Nutrition Indices" OR "Nutritional Index" OR "Index, Nutritional" OR "Indices, Nutritional" OR "Nutritional Indices" OR "Nutrition Index" OR "Index, Nutrition" OR "Indices, Nutrition" OR "Prognostic Nutritional Index" OR "Index, Prognostic Nutritional" OR "Indices, Prognostic Nutritional" OR "Nutritional Index, Prognostic" OR "Prognostic Nutritional Indices" OR "Mini Nutritional Assessment" OR "Assessment, Mini Nutritional" OR "Assessments, Mini Nutritional" OR "Mini Nutritional Assessments" OR "Nutritional Assessment, Mini" OR "Nutritional Assessments, Mini" OR "Mini Nutrition Assessment" OR "Assessment, Mini Nutrition" OR "Assessments, Mini Nutrition" OR "Mini Nutrition Assessments" OR "Nutrition Assessment, Mini" OR "Nutrition Assessments, Mini") Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos OR AB=("Nutrition Assessment" OR "Assessments, Nutrition" OR "Nutrition Assessments" OR "Nutritional Assessment" OR "Assessment, Nutritional" OR "Assessments, Nutritional" OR "Nutritional Assessments" OR "Assessment, Nutrition" OR "Nutrition Indexes" OR "Indexes, Nutrition" OR "Nutrition Indices" OR "Nutritional Index")</p>

OR "Index, Nutritional" OR "Indices, Nutritional" OR "Nutritional Indices" OR "Nutrition Index" OR "Index, Nutrition" OR "Indices, Nutrition" OR "Prognostic Nutritional Index" OR "Index, Prognostic Nutritional" OR "Indices, Prognostic Nutritional" OR "Nutritional Index, Prognostic" OR "Nutritional Indices, Prognostic" OR "Prognostic Nutritional Indices" OR "Mini Nutritional Assessment" OR "Assessment, Mini Nutritional" OR "Assessments, Mini Nutritional" OR "Mini Nutritional Assessments" OR "Nutritional Assessment, Mini" OR "Nutritional Assessments, Mini" OR "Mini Nutrition Assessment" OR "Assessment, Mini Nutrition" OR "Assessments, Mini Nutrition" OR "Mini Nutrition Assessments" OR "Nutrition Assessment, Mini" OR "Nutrition Assessments, Mini") Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos AND AB=("heart failure" OR "Cardiac Failure" OR "Heart Decompensation" OR "Decompensation, Heart" OR "Heart Failure, Right-Sided" OR "Right-Sided Heart Failure" OR "Myocardial Failure" OR "Congestive Heart Failure" OR "Heart Failure, Congestive" OR "Heart Failure, Left-Sided" OR "Left-Sided Heart Failure" OR "HF" OR "ventricular failure") Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos

Supplementary Table 1. Excluded studies after full-text analysis

Author	Title	Reason for exclusion
Agus et al.	Prognostic nutritional index predicts one-year outcome in heart failure with preserved ejection fraction	Participants
Al-najar et al.	Predicting Outcome in Patients With Left Ventricular Systolic Chronic Heart Failure Using a Nutritional Risk Index	Participants
Arikbuka et al.	Assessment of nutritional status and its association with anthropometric measurements, blood results and body composition in elderly cardiovascular patients	Outcome/participants
Asai et al.	Prognosis value of the mini nutritional assessment short form tool in outpatients with heart failure with mid-range ejection fraction	Outcome
Barge-Caballero et al.	Valor pronóstico del índice de riesgo nutricional en receptores de trasplante cardiaco TT - Prognostic value of the nutritional risk index in heart transplant recipients	Duplicate
Bilgen et al.	Insufficient Calorie Intake Worsens Post-Discharge Quality of Life and Increases Readmission Burden in Heart Failure	Participants
Bonilla-Palomas et al.	[Impact of malnutrition on long-term mortality in outpatients with chronic heart failure]. TT - Influencia de la desnutrición sobre la mortalidad a largo plazo en pacientes ambulatorios con insuficiencia cardiaca crónica.	Participants
Bonilla-Palomas et al.	Impact of nutritional status on middle term mortality of patients with heart failure	Full-text not available
Bonilla-Palomas et al.	Does malnutrition determined by the Mini Nutritional Assessment (MNA) test retain its influence on long-term mortality in hospitalized patients with heart failure?	Full-text not available
Bonilla-Palomas et al.	Prevalence of undernutrition determined by the Mini Nutritional Assessment (MNA) and its impact on medium-term mortality in hospitalized patients with heart failure	Abstract
Broqvist et al.	Nutritional assessment and muscle energy metabolism in severe chronic congestive heart failure--effects of long-term dietary supplementation.	Exposure
Dereli et al.	Effects of sacubutril/valsartan on nutritional status in heart failure with reduced ejection fraction.	Exposure
Duarte et al.	Is there an association between the nutritional and functional parameters and congestive heart failure severity?	Design/outcome
Duarte et al.	Adductor pollicis muscle and nutritional status in heart failure patients: Is there an association?	Design/outcome
Fatyga et al.	Should malnutrition risk be assessed in older patients with elevated levels of NT-proBNP?	Design/outcome
Figueiredo et al.	Nutritional risk in heart failure-a retrospective study	Abstract/poster
Formiga et al.	Functional outcomes of elderly patients after the first hospital admission for decompensated heart failure (HF). A prospective study.	Design/outcome
Genev et al.	Improved Nutrition Status in Patients With Advanced Heart Failure Implanted With a Left Ventricular Assist Device	Outcome
Genev et al.	Improved nutritional status in patients with advanced heart failure following left ventricular assist device implantation	Outcome
Gomez-Lopez et al.	Markers of malnutrition in hospitalized patients with heart failure	Full-text not available
Gonzalez et al.	Quick screening of nutritional status in an outpatient heart failure unit using de mini nutritional assessment short form tool	Abstract/poster
Gonzalez Ferreiro et al.	Nutritional assessment and prognosis in hospitalized patients with acute heart failure	Full-text not available

Gouya et al.	Association of nutritional risk index with metabolic biomarkers, appetite-regulatory hormones and inflammatory biomarkers and outcome in patients with chronic heart failure	Participants
Guerra-Sanchez et al.	Efecto de una intervención nutricional doble sobre el estado nutricional, la capacidad funcional y la calidad de vida de pacientes con insuficiencia cardiaca crónica: resultados a los 12 meses de un ensayo clínico aleatorizado	Design
Guerra-Sanchez et al.	[Nutritional screening in heart failure patients: 5 methods review]. TT - Cribado nutricional en pacientes con insuficiencia cardiaca: análisis de 5 métodos.	Design
Gulatava et al.	; ASPECTS OF NUTRITION IN PATIENTS WITH CONGESTIVE HEART FAILURE	Full-text not available
Harada et al.	The nutritional index 'conut' is useful for predicting prognosis of acute decompensated heart failure	Abstract/poster
Ielli et al.	Nutritional status is associated with physical function and disability in older adults with chronic heart failure	Design/Outcome
Ielli et al.	Association between nutritional status and outcomes in older adults affected by heart failure	Abstract/poster
Iwakami et al.	A useful risk assessment tool of malnutrition and its prognostic impact in patients with acute heart failure	Full-text not available
Joaquín et al.	Mini nutritional assessment is a better predictor of mortality than subjective global assessment in heart failure out-patients.	Participants
Joaquín et al.	Mini Nutritional Assessment Short Form is a morbi-mortality predictor in outpatients with heart failure and mid-range left ventricular ejection fraction.	Participants
Karst et al.	Relationship between adductor pollicis muscle thickness and subjective global assessment in a cardiac intensive care unit.	Design/Outcome
Katano et al.	Nutritional status and energy intake as predictors of functional status after cardiac rehabilitation in elderly inpatients with heart failure — A retrospective cohort study	Outcome
Katano et al.	Assessment of both energy intake and nutritional status predicts functional recovery after cardiac rehabilitation in elderly inpatients with heart failure	Abstract/poster
Kawata et al.	Prognostic nutrition index predicts prognosis in ultra-elderly patients with heart failure	Abstract/poster
Keisuke et al.	Usefulness of nutritional assessment using controlling nutritional status score at admission and short-term prognosis in elderly patients with acute heart failure	Language
Kitamura et al.	Differences in nutritional status and activities of daily living and mobility in elderly hospitalized patients with heart failure.	Outcome
Kootaka et al.	The GLIM criteria for defining malnutrition can predict physical function and prognosis in patients with cardiovascular disease	Exposure
Krzysztofak et al.	Correlation of nutritional status with chosen biochemical parameters in patients hospitalized due to heart failure with reduced ejection fraction	Full-text not available
Krzysztofak et al.	Prognostic value of nutritional status in patients diagnosed with heart failure with reduced ejection fraction (HFrEF)-single center pilot study	Abstract/poster
Kubo et al.	Factors delaying the progress of early rehabilitation of elderly Japanese patients with heart failure.	Outcome
Lilamand et al.	Quality of life, physical performance and nutritional status in older patients hospitalized in a cardiology department	Design/outcome
Lopez-Rodriguez et al.	Nutritional status in heart failure patients with coexisting kidney disease	Full-text not available

Matsuo et al.	Risk of malnutrition is associated with poor physical function in patients undergoing cardiac rehabilitation following heart failure	Design/outcome
Migaj et al.	Malnutrition risk in heart failure with reduced ejection fraction patients-single center/pilot study	Abstract/poster
Minamisawa et al.	Geriatric nutritional risk index predicts cardiovascular events in patients at risk for heart failure	Participants
Morimoto et al.	Association of lower extremity function with nutritional status and number of drugs in patients with chronic heart failure	Design
Nochioka et al.	Nutritional status and prognosis of stage-B patients	Full-text not available
Ono et al.	Geriatric nutritional risk index at hospital discharge is a useful predictor of adverse outcome in hospitalized patient with acute decompensated heart failure	Abstract/poster
Pachon et al.	Nutritional status and its impact on mortality in patients with heart failure with preserved or depressed systolic function, are there differences?	Abstract/poster
Perez Ruiz et al.	Impact of nutritional assessment in patients with heart failure	Full-text not available
Pilotto et al.	Multidimensional Prognostic Index based on a comprehensive geriatric assessment predicts short-term mortality in older patients with heart failure.	Exposure
Plas et al.	Comparison of screening tools for malnutrition in chronic heart failure patients	Full-text not available
Racca et al.	End-stage heart failure: Two surgical approaches with different rehabilitative outcomes	Outcome
Saez Rubio et al.	Nutritional status in people with chronic heart failure and / or chronic obstructive pulmonary disease. Impact on quality of life and exacerbations	Full-text not available
Saitoh et al.	Nutritional status and its effects on muscle wasting in patients with chronic heart failure: insights from Studies Investigating Co-morbidities Aggravating Heart Failure	Participants
Sargento et al.	Geriatric nutritional risk index as a nutritional and survival risk assessment tool in stable outpatients with systolic heart failure.	Participants
Sargento et al.	Nutritional status of geriatric outpatients with systolic heart failure and its prognostic value regarding death or hospitalization, biomarkers and quality of life.	Participants
Satendra et al.	The relation between malnutrition evaluated by the Mini-Nutritional Assessment (MNA) in ambulatory patients with heart failure, quality of life (QOL) assessed by the MLHFQ test and NtProBNP	Full-text not available
Sattler et al.	Association between the prognostic nutritional index and dietary intake in community-dwelling older adults with heart failure: Findings from NHANES III	Design/Outcome
Selan et al.	IMPACT OF NUTRITIONAL STATUS AND SLEEP QUALITY ON HOSPITAL UTILISATION IN THE OLDEST OLD WITH HEART FAILURE	Outcome
Seo et al.	Prognostic Significance of Serum Cholinesterase Level in Patients With Acute Decompensated Heart Failure With Preserved Ejection Fraction: Insights From the PURSUIT-HFpEF Registry.	Outcome
Shimoyama et al.	Geriatric nutritional risk index and 100-m walk achievement predict discharge to home in elderly patients with heart failure.	Outcome
Shirakabe et al.	Characteristics of Patients with an Abnormally Decreased Plasma Xanthine Oxidoreductase Activity in Acute Heart Failure Who Visited the Emergency Department.	Outcome
Shirakabe et al.	Prognostic Value of Both Plasma Volume Status and Nutritional Status in Patients With Severely Decompensated Acute Heart Failure	Exposure

Silva et al.	Perfil nutricional de portadores de doenças cardiovasculares internados em um hospital: estudo prospectivo TT - Perfil nutricional de los pacientes con enfermedad cardiovascular en un hospital: estudio prospectivo TT - Nutritional profile of cardiovascular disease bearing patients under hospitalization: a prospective study	Participants/Exposure
Son et al.	High nutritional risk is associated with worse health-related quality of life in patients with heart failure beyond sodium intake.	Outcome
Sun et al.	Elderly chronic heart failure patients with sarcopenia had lower MNA-SF scores and lower serum albumin level	Abstract/poster
Sundararajan et al.	Objective Nutritional Index is Associated with Worse Cardiopulmonary Exercise Test Performance in Advanced Heart Failure Patients	Abstract/poster
Sundararajan et al.	Assessing Malnutrition Using Nutritional Risk Index Predicts Mortality after Left Ventricular Assist Device Implantation in Patients with End Stage D Heart Failure	Abstract/poster
Supressa et al.	Assessment of nutritional status in patients hospitalized for heart failure and for respiratory failure	Full-text not available
Suzuki et al.	Evaluation of useful and convenient screening methods for cardiac cachexia in outpatients with heart failure	Abstract/poster
Suzuki et al.	MINI NUTRITIONAL ASSESSMENT SHORT FORM AND KIHON CHECKLIST ARE SIMPLE AND USEFUL SCREENING FOR CARDIAC CACHEXIA IN OUTPATIENTS WITH HEART FAILURE	Abstract/poster
Suzuki et al.	Heart failure symptoms, handgrip strength and nutritional status have an impact on frailty in outpatients with chronic heart failure in Japan	Full-text not available
Sze et al.	Evaluation of malnutrition using 6 screening tools in patients with chronic heart failure	Full-text not available
Sze et al.	Malnutrition, congestion and mortality in ambulatory patients with heart failure	Participants
Sze et al.	Prevalence and Prognostic Significance of Malnutrition Using 3 Scoring Systems Among Outpatients With Heart Failure: A Comparison With Body Mass Index.	Participants
Sze et al.	The impact of malnutrition on short-term morbidity and mortality in ambulatory patients with heart failure.	Participants
Sze et al.	The efficacy of malnutrition tools in detecting malnutrition and predicting mortality in patients with chronic heart failure	Abstract/poster
Sze et al.	Agreement and Classification Performance of Malnutrition Tools in Patients with Chronic Heart Failure	Outcome
Tevik et al.	Nutritional risk screening in hospitalized patients with heart failure.	Design/outcome
Tse et al.	Multi-modality machine learning approach for risk stratification in heart failure with left ventricular ejection fraction ≤ 45 .	Outcome
Yalinkiliç et al.	Determination of frailty in elderly individuals with heart failure	Language
Yamada et al.	Nutritional assessment by prognostic nutritional index provides the additional long-term prognostic information to body mass index in patients admitted with acute decompensated heart failure	Abstract/poster
Yamauti et al.	Subjective global assessment of nutritional status in cardiac patients.	Design
Yano et al.	Distinct determinants of muscle wasting in nonobese heart failure patients with and without type 2 diabetes mellitus	Design
Yasuhara et al.	Energy Metabolism and Nutritional Status in Hospitalized Patients with Chronic Heart Failure.	Design/Outcome

Yasumura et al.	Nutritional assessment indices in heart failure with and without reduced exercise tolerance	Abstract/poster
Zamora et al.	Prognosis value of the mini nutritional assessment short form tool in outpatients with heart failure with mid-range ejection fraction	Abstract/poster

Supplementary Table 2. Research Quality Scores: Ottawa–Newcastle Assessment Scale (ONS).

Reference	Tool	NOS score [Evidence]
Katano et al., 2021	MNA-SF	8
Boixader et al., 2016	CONUT; MNA-SF	6
Martín-Sánchez et al., 2019	MNA-SF	7
Yost et al., 2014	MNA; MNA-SF	5
Guerra-Sánchez et al., 2015	SGA; MNA	3
Kaluzna-Olestky et al., 2020	MNA	5
Bonilla-Palomas et al., 2011	MNA	8
Suzuki et al., 2015	MNA	6
Aggarwal et al., 2013	MNA	8
Kinugasa et al., 2013	GNRI	8
Kitamura et al., 2019	GNRI	6
Hirose et al., 2020	GNRI	7
Nakamura et al., 2019	GNRI	7
Honda et al., 2016	GNRI	5
Nishi et al., 2019	GNRI	8
Minamisawa et al., 2019	GNRI	8
Ishiwata et al., 2020	GNRI	6
Cheng et al., 2017	PNI	9
Candeloro et al., 2020	PNI	5
Çinier et al., 2020	PNI	8
Yost et al., 2017	PNI	5
Nishi et al., 2017	CONUT	7
Nishi et al., 2017	CONUT	7
Iwakami et al., 2016	CONUT	8
Saito et al., 2020	CONUT	6
La Rovere et al., 2016	CONUT	6
Takikawa et al., 2021	CONUT	6
Uribarri et al., 2018	NRI	6
Cho et al., 2018	NRI	7
Aziz et al., 2011	NRI	9
Barge-Caballero et al., 2017	NRI	8
Adejumo et al., 2015	NRI	6
Shirakabe et al., 2017	PNI; CONUT	7
Chien et al., 2019	PNI; CONUT; GNRI	9
Uemura et al., 2020	GNRI; CONUT	8
Sze et al., 2017	PNI; CONUT; GNRI	7
Alatas et al., 2020	PNI; CONUT; GNRI	8
Horiuchi et al., 2017	GNRI; CONUT	7
Narumi et al., 2013	PNI; CONUT; GNRI	8
Seo et al., 2019	PNI; CONUT; GNRI	7
Yoshihisa et al., 2017	PNI; CONUT; GNRI	9
Tevik et al., 2016	NRS-2002	7

CONUT: Controlling Nutritional Status; GNRI: Geriatric nutritional risk index; MNA: Mini Nutritional Assessment; MNA-SF: Mini Nutritional Assessment Short Form; NRI: Nutritional Risk Index; NRS-2002: Nutritional Risk Screening; PNI: Prognostic nutritional index; SGA: Subjective Global Assessment;

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8. CONSIDERAÇÕES FINAIS

Redigir um trabalho científico é um desafio para qualquer pessoa, independente de sua complexidade. Exige pesquisa, organização, dedicação e priorização. Embora não seja o foco principal da residência multiprofissional em saúde, o trabalho de conclusão (TCR) contribui imensamente para a formação profissional. Durante a execução deste trabalho, me vi dedicada a pensar sobre novas formas de triar e avaliar nutricionalmente pacientes hospitalizados por IC. Questionei-me sobre formas para que uma eventual ferramenta possa alcançar níveis de acurácia abrangentes e impactar em desfechos importantes como qualidade de vida, rehospitalização e mortalidade, além de reduzir custos para o sistema único de saúde (SUS), cujos recursos são extremamente limitados.

Os resultados apresentados nesta revisão demonstraram que as ferramentas multidimensionais utilizadas nos dias atuais para triagem e avaliação nutricional em pacientes hospitalizados por IC apresentam bom valor prognóstico e aplicabilidade clínica, especialmente no que diz respeito a risco de mortalidade. No entanto, pôde-se observar alta heterogeneidade quanto à prevalência de desnutrição avaliada pelas diferentes ferramentas. Diante disso, evidencia-se a necessidade de que estudos mais robustos aprofundem-se no desenvolvimento de uma única ferramenta, completa e acurada, afim de estabelecer um método padrão ouro, que possa ser utilizado a nível nacional e internacional, evitando possíveis equívocos de identificação e prognóstico clínico indesejado.

Embora conte com algumas limitações, como os diferentes pontos de corte utilizados pelas ferramentas e o tamanho de amostra de alguns estudos que culminam em menor poder estatístico, esta parece ser a primeira revisão sistemática e meta-análise a avaliar o valor prognóstico dos instrumentos de triagem e avaliação nutricional com foco especificamente em pacientes hospitalizados por IC.

Portanto, devido à extrema relevância de explorar potenciais formas para prever desfechos clínicos importantes, como hospitalização e mortalidade, e do elevado risco apresentado por essa população, esta revisão cumpre seu objetivo, uma vez que fornece novas evidências que podem auxiliar na prática clínica, como qual ferramenta mostrou-se mais adequada para triagem nutricional de pacientes hospitalizados por IC, a forma que as ferramentas atuais divergem no que diz respeito a detecção de risco de desnutrição ou diagnóstico de desnutrição, e qual a associação destas ferramentas com desfechos de hospitalização e mortalidade, o que até o momento não havia sido feito.