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CUIDADO NUTRICIONAL DO PACIENTE CRÍTICO:
Avaliação das diretrizes para a prática clínica a partir das ferramentas AGREE II e
AGREE-REX

Porto Alegre

2021

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AGREE-REX**

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Orientadora: Profa. Dra. Flávia Moraes Silva

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Dedico esse trabalho aos pacientes que necessitam de atendimento em unidades de terapia intensiva e aos profissionais de saúde dessa área que atuam incansavelmente na perspectiva de associar evidências científicas à atenção integral do indivíduo.

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*“Você pode desperdiçar a vida criando limites. Ou você pode
vivê-la ultrapassando-os”*

Shonda Rhimes

LISTA DE SIGLAS

AGREE II	<i>Advancing Guideline Development, Reporting and Evaluation in Health Care II</i>
AGREE-REX	<i>AGREE-Recommendation Excellence</i>
AND	<i>Academy of Nutrition and Dietetics</i>
ASG	<i>Avaliação Subjetiva Global</i>
ASPEN	<i>American Society for Parenteral and Enteral Nutrition</i>
BRASPEN	<i>Sociedade Brasileira de Nutrição Enteral e Parenteral</i>
CPG	<i>Clinical Practice Guidelines</i>
DGEM	<i>German Society for Nutritional Medicine</i>
ESICM	<i>European Society of Intensive Care Medicine</i>
ESPEN	<i>European Society for Clinical Nutrition and Metabolism</i>
IOM	<i>Institute of Medicine</i>
NRS-2002	<i>Nutritional Risk Screening</i>
NUTRIC	<i>Nutrition Risk in the Critically ill</i>
SCCM	<i>Society of Critical Care Medicine</i>
SEMICYUC	<i>Spanish Society of Intensive Care Medicine and Coronary Units</i>
SENPE	<i>Spanish Society of Parenteral and Enteral Nutrition</i>
SFAR	<i>Société française d'anesthésie et de réanimation</i>
UTI	<i>Unidades de Terapia Intensiva</i>

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FORMATO DA DISSERTAÇÃO

Esta dissertação foi desenvolvida com base na Normativa de instrução para trabalho final do Programa de Pós-graduação em Ciências da Nutrição da Universidade Federal de Ciências da Saúde de Porto Alegre, a qual pode ser consultada no site institucional (<https://www.ufcspa.edu.br/documentos/ppg/nutricao/normativa-instrucao-trabalho-final.pdf>).

O produto desta dissertação compreende o artigo científico original, detalhado abaixo:

- *Quality appraisal of clinical nutrition practice guidelines for adult critically ill patient: a systematic review using AGREE II and AGREE-REX Instruments* - o qual foi submetido ao periódico *Nutrition Reviews* (ISSN: 1753-4887; fator de impacto: 7.110, qualis A1), cujas normas para submissão podem ser consultadas em: https://academic.oup.com/nutritionreviews/pages/General_Instructions

RESUMO

Fundamentação: O cuidado nutricional do paciente crítico deve seguir a prática baseada em evidência, sendo as diretrizes de prática clínica desenvolvidas por sociedades de nutrição e de terapia intensiva amplamente utilizadas por profissionais da área como norteadores da tomada de decisões para esse cuidado. Contudo, para que as diretrizes e suas recomendações possam ser confiáveis é necessário que apresentem qualidade, a qual pode ser avaliada por ferramentas específicas como o *Advancing Guideline Development, Reporting and Evaluation in Health Care II* (AGREE II) e *AGREE-Recommendation Excellence* (AGREE-REX).

Objetivo: O presente estudo teve como objetivos: 1. Revisar sistematicamente a literatura acerca de diretrizes para a prática do cuidado nutricional de pacientes críticos; 2. Avaliar criticamente a qualidade metodológica e das recomendações dessas diretrizes; 3. Avaliar a concordância das recomendações estabelecidas pelas diretrizes.

Método: Foi realizada uma revisão sistemática (protocolo número CRD42020184199) de diretrizes acerca das etapas do cuidado nutricional do paciente crítico adulto/idoso. A busca da literatura foi conduzida no Pubmed, Embase, Cochrane Library e outras quatro bases de dados específicas de diretrizes até junho de 2021. Dois revisores independentemente, avaliaram títulos e resumos e realizaram a leitura do texto completo das diretrizes potencialmente elegíveis para determinar ou não sua inclusão e coletaram dados de interesse através de uma ficha padronizada. Divergências foram resolvidas por um terceiro revisor. Subsequentemente, quatro revisores avaliaram a qualidade das diretrizes usando a ferramenta AGREE II e das recomendações com o suporte da ferramenta AGREE-REX. As diretrizes foram classificadas em recomendadas, recomendadas com modificações ou não recomendadas a partir do escore global obtido no AGREE II. Nas diretrizes classificadas como tendo qualidade moderada ou superior foi avaliada a qualidade das recomendações, a qual foi classificada como baixa, moderada ou alta a partir do escore global obtido no AGREE-REX. Foi calculada a frequência relativa da concordância entre as diretrizes acerca das recomendações estabelecidas para as diferentes etapas do cuidado nutricional.

Resultados: Nove diretrizes de terapia nutricional para pacientes críticos foram identificadas. A média do escore global para o AGREE II foi igual a $3,5 \pm 1,4$. Nenhuma das diretrizes apresentou escore global de qualidade $> 80\%$, duas apresentaram escore entre 60-79% e cinco apresentaram escore global de qualidade $< 40\%$. Apenas a *Academy of Nutrition and Dietetics* e *European Society of Intensive Care Medicine* tiveram uma qualidade global aceitável e foram recomendadas para uso na prática diária de acordo com o AGREE II. O domínio que

apresentou maior escore entre as diretrizes foi o de "clareza da apresentação", enquanto que o domínio "aplicabilidade" foi o que apresentou o menor escore. Em sete diretrizes o domínio "rigor metodológico" apresentou escore menor do que 60%. Nenhuma das recomendações das quatro diretrizes com qualidade moderada/alta apresentou escore de qualidade global acima de 70%, sendo os seus conjuntos de recomendações classificados como de moderada qualidade de acordo com o AGREE-REX. As principais recomendações para cada etapa do processo de cuidado nutricional para pacientes críticos foram baseadas no consenso de especialistas e para a maioria delas a frequência de concordância entre as diretrizes foi menor ou igual a 50%.

Conclusão: A maioria das diretrizes para a prática do cuidado nutricional de pacientes críticos atingiu escore global de qualidade abaixo de 40% e apenas duas atingiram qualidade aceitável e podem ser recomendadas de acordo com o AGREE II. De acordo com o AGREE-REX as recomendações das diretrizes apresentam qualidade moderada. A maioria das recomendações sobre as etapas do cuidado nutricional do paciente crítico é baseada em consenso de especialistas e a concordância entre as diretrizes foi igual ou inferior a 50% para a maior parte delas. Tais achados demonstram que a forma como as diretrizes para cuidado nutricional do paciente crítico estão apresentadas requer melhorias e que a área de nutrição no paciente crítico carece de estudos primários bem delineados para que as recomendações possam ser estabelecidas com base em evidências científicas com maior poder para testar hipóteses.

Palavras-chave: Cuidados Críticos; Unidades de Terapia Intensiva; Diretriz de Prática Clínica; Terapia Nutricional; Avaliação da Qualidade dos Cuidados de Saúde.

ABSTRACT

Background: Nutritional therapy should follow evidence-based practice, being the Clinical Practice Guidelines (CPG) developed by societies of nutrition and intensive care widely used by health professionals as decision-making guides for this care. However, in order CPG and their recommendations to be reliable, it is necessary that they present quality, which can be evaluated by specific tools such Advancing Guideline Development, Reporting and Evaluation in Health Care II (AGREE II) and AGREE-Recommendation Excellence (AGREE-REX).

Aims: This study aimed to: 1. Systematically review the literature about nutrition CPG for critically ill patients; 2. Critically assess the methodological and recommendations quality of these CPGs; 3. Assess the agreement of recommendations established by the CPG.

Methods: A systematic review was performed (protocol number CRD42020184199) about CPG of nutrition care process of adult and elderly critically ill patients. Search was conducted on Pubmed, Embase, Cochrane Library, and other four specific databases of guidelines was conducted up to June 2021. Two reviewers independently assessed titles and abstracts and read the full text of potentially eligible guidelines to determine whether or not they were included and collected data of interest through a standardized form. A third reviewer resolved disagreements. Subsequently four reviewers appraised the guidelines quality using the AGREE II and AGREE-REX. CPGs were classified as recommended, recommended with modifications or not recommended based on the global score obtained in AGREE II. In those CPGs classified as having moderate or superior quality, the quality of the recommendations was evaluated, which was classified as low, moderate or high based on the global score obtained in AGREE-REX. The relative frequency of agreement between the CPGs recommendations established for the different stages of nutritional care was calculated.

Results: Nine CPG for nutrition in critically ill patients were identified. Mean global score in AGREE II was 3.5 ± 1.4 . None of the CPG had an overall quality score $> 80\%$, two had a score between 60-79% and five had an overall quality score $< 40\%$. Only Academy of Nutrition and Dietetics and European Society of Intensive Care Medicine had a total acceptable quality and were recommended for daily practice according AGREE-II. The domain with the highest score among the CPG was "clarity of presentation", while the domain "applicability" had the lowest score. In seven CPG the domain "rigor of development" had a score lower than 60%. None of the four CPG with overall quality moderate/high recommendations had an overall quality score above 70%, thus being their sets of

recommendations classified as moderate quality according AGREE-REX. The major recommendations for each step of nutrition care process for critically ill patients were based on expert consensus and for most of them, the frequency of agreement between the guidelines was less than or equal to 50%.

Conclusion: Most nutrition care CPG for critically ill patients reached an overall quality score below 40% and two attained acceptable quality and can be recommended according to the AGREE II. According to AGREE-REX, the guideline recommendations are of moderate quality. Most recommendations about nutritional care steps for critically ill patients are based on expert consensus and agreement between guidelines was less than or equal 50% for most of them. These findings demonstrate that the way nutrition CPGs for critically ill patients are presented requires improvements and that the area of nutrition in critically ill patients lacks of well-designed primary studies for that the recommendations can be established based on scientific evidence with greater power to test hypotheses.

Keywords: Critical care; Intensive care unit; Practice guidelines; Nutrition therapy; Health Care Quality Assessment.

3 REFERENCIAL TEÓRICO

O presente referencial teórico aborda aspectos relacionados ao cuidado nutricional do paciente crítico, às diretrizes clínicas e à avaliação da sua qualidade.

3.1 CUIDADO NUTRICIONAL DO PACIENTE CRÍTICO

O paciente crítico é definido como o indivíduo que cursa com uma doença de alta severidade, envolvendo uma ou mais disfunções orgânicas, necessitando de intervenções invasivas de suporte de vida¹. Como característica principal, esse paciente apresenta uma resposta metabólica ao estresse envolvendo componentes neuroendócrinos, inflamatórios e imunológicos que são adaptados para que o mesmo possa sobreviver à doença aguda. A liberação de citocinas pró-inflamatórias (fatores de necrose tumoral, interleucina-1 e interleucina-6) acionam sintomas como anorexia a nível hipotalâmico, induzem uma acentuada degradação muscular - envolvendo perda de função e contratilidade muscular, e geram alterações fisiológicas que culminam com intensa proteólise e lipólise. Outras alterações como hiperglicemia e resistência à ação da insulina relacionada ao estresse ocorrem visando garantir substrato energético necessário para manutenção de órgãos vitais não insulino dependentes^{2,3}.

Como consequência clínica desta resposta, em diversos estágios da doença crítica, há alteração no metabolismo e na absorção de nutrientes no trato gastrointestinal e no meio intracelular, além de modificação da oxidação de substratos. Além disso, também ocorre degradação excessiva de proteína e balanço nitrogenado negativo levando a depleção do tecido muscular. Essas alterações sofrem influência de adaptações fisiológicas (febre, oscilação de frequência cardíaca, agitação), bem como de intervenções terapêuticas (uso de sedativos e bloqueadores neuromusculares)^{2,3}. A doença crítica cursa, por conseguinte, com repercussões importantes no gasto energético e na composição corporal do paciente, sendo o catabolismo descontrolado determinante de um inevitável comprometimento do estado nutricional².

De fato, uma revisão sistemática conduzida pelo nosso grupo de pesquisa incluindo 36 estudos observacionais demonstrou que pacientes críticos frequentemente apresentam risco nutricional, sendo que a prevalência dessa condição pode chegar a até 99,5%⁴. Ainda, revisão sistemática incluindo 20 estudos demonstrou que a desnutrição também é altamente prevalente em Unidades de Terapia Intensiva (UTI) podendo atingir até 82% dos pacientes⁵.

Cabe ressaltar que tanto o risco nutricional como a desnutrição são preditores de desfechos clínicos desfavoráveis em pacientes críticos, estando associados a maior mortalidade, a tempo de internação hospitalar e em UTI prolongados, bem como a maior tempo de ventilação mecânica^{4,5}.

Contudo, atualmente ainda é comum a dificuldade em sistematizar e instituir o cuidado nutricional do paciente crítico em decorrência da complexidade da sua resposta metabólica e da diversidade da fisiopatologia das diferentes doenças que o levam para a UTI². O cuidado nutricional pode ser dividido em quatro principais etapas distintas, mas complementares: 1. avaliação nutricional; 2. diagnóstico nutricional; 3. intervenção nutricional; 4. Monitoramento⁶. As etapas do cuidado nutricional para diferentes condições clínicas, inclusive para o paciente crítico, são sumarizadas em diretrizes de prática clínica que embasam a tomada de decisões dos profissionais de saúde sobre cuidados de saúde apropriados para pacientes e circunstâncias específicas.

3.2 DIRETRIZES CLÍNICAS

Com o rápido crescimento do conhecimento e publicações em saúde, e com a consciência de que muitas vezes as evidências geradas sofrem importante influência de vieses e não são aplicáveis à prática, as diretrizes apresentam-se como alternativas assertivas de suporte para a tomada de decisões. Nestes documentos preconiza-se que a evidência científica seja avaliada criticamente e sintetizada seguindo um rigoroso processo⁷. De acordo com o *Institute of Medicine* (IOM)⁷, diretrizes de prática clínica representam declarações que incluem recomendações destinadas a otimizar a assistência ao paciente que são geradas através de uma revisão sistemática de evidências e uma avaliação dos riscos e benefícios das opções de cuidados alternativos.

Para ser confiável, uma diretriz de prática clínica deve cumprir etapas específicas no seu processo de desenvolvimento. Como primeiro passo define-se um tópico de interesse e seleciona-se um grupo multidisciplinar de especialistas (incluindo metodologista) e representantes da população-alvo. *A priori*, é de suma importância o manejo de possíveis conflitos de interesse dos profissionais envolvidos na elaboração da diretriz. O seu desenvolvimento deve ser baseado em uma revisão sistemática da literatura, incluindo todas as etapas recomendadas, ou seja: definição das perguntas de pesquisa no formato PICO/PECO, busca abrangente e sensível de estudos, definição dos desfechos de interesse e plano de análises, seleção dos estudos e extração de dados por pares, avaliação do risco de viés, e

síntese dos resultados⁷⁻⁹. Além disso, este processo deve ser transparente, minimizando distorções e vieses e deve considerar valores e preferências dos pacientes e/ou familiares. A etapa de formulação de recomendações deve prover um raciocínio lógico da relação entre alternativas de cuidado e desfechos em saúde, disponibilizando informações acerca da avaliação da qualidade da evidência e força de recomendação. Um raciocínio subjacente à recomendação deve ser disponibilizado. Ademais, as recomendações devem ser articuladas de forma padronizada, detalhando precisamente qual é a ação recomendada, e em que circunstâncias deve ser executada. Na etapa de finalização da diretriz deve-se garantir uma revisão externa prévia a sua publicação, para posteriormente seguir as etapas de disseminação e comunicação. A atualização da mesma deve ser realizada periodicamente na disponibilidade de novas evidências que justificam modificações das recomendações^{7,8}.

Contudo, mesmo na disponibilidade de guias para elaboração de diretrizes, a qualidade do processo de desenvolvimento e a adesão do grupo de desenvolvedores aos padrões de qualidade permanece frequentemente insatisfatória e não confiável nas diferentes áreas⁷. Sendo assim, foram propostos instrumentos padronizados para a avaliação da qualidade de diretrizes e suas recomendações. Em 2003 um grupo internacional de pesquisadores e desenvolvedores de diretrizes propuseram o programa *Appraisal of Guidelines for Research & Evaluation* (AGREE) com o intuito de contribuir para a construção de diretrizes¹⁰. O mesmo consiste em um portfólio de instrumentos orientativos para condução das etapas de desenvolvimento até avaliação da qualidade de diretrizes, norteando ainda como as informações devem ser reportadas¹¹.

Uma revisão sistemática da literatura identificou 40 instrumentos disponíveis para avaliação da qualidade de diretrizes¹², porém o AGREE II ainda é o mais amplamente utilizado¹¹. Fato esse observado em uma revisão sistemática que identificou 118 publicações que aplicaram o AGREE II em diretrizes clínicas com o objetivo de investigar como é realizada a pontuação dos domínios pelos revisores e qual o principal domínio considerado para avaliação da qualidade das diretrizes¹³. O AGREE II aborda o processo de construção de uma diretriz bem como a variabilidade na sua qualidade. Ou seja, avalia o rigor metodológico e transparência do processo de desenvolvimento. O instrumento contempla seis domínios, sendo que cada um capta pontos específicos da qualidade da diretriz. Estes domínios são compostos por um total de 23 itens-chave seguidos de dois itens de classificação e avaliação global, os quais estão apresentados na **Tabela 1**¹⁴. Os 23 itens podem ser consultados no Material do Usuário traduzido para o português, disponível pelo link https://www.agreetrust.org/wpcontent/uploads/2013/06/AGREE_II_Brazilian_Portuguese.pdf

ou no website <https://www.agreetrust.org/agree-ii/>, no qual pode ser acessado o material referente ao instrumento e ser realizado um treinamento para a sua aplicação.

Tabela 1 – Descrição dos domínios e itens que compõe o AGREE II

Domínio	Itens	Descrição
1) Escopo e finalidade	1-3	Diz respeito ao objetivo geral da diretriz, às questões específicas de saúde e à população-alvo
2) Envolvimento das partes interessadas	4-6	Foca em que medida a diretriz foi desenvolvida pelas partes interessadas adequadas e representa a visão dos usuários pretendidos
3) Rigor do desenvolvimento	7-14	Diz respeito ao processo usado para coletar e sintetizar as evidências, os métodos para a formulação das recomendações e sua respectiva atualização
4) Clareza da apresentação	15-17	Aborda a linguagem, estrutura e o formato da diretriz
5) Aplicabilidade	8-21	Foca em prováveis fatores facilitadores e barreiras para a implementação, estratégias para melhorar a aplicação, bem como envolvimento de recursos relacionados à utilização da diretriz
6) Independência editorial	22-23	Diz respeito à formulação das recomendações de modo a não terem vieses decorrentes de interesses conflitantes

Fonte: Adaptada de AGREE Next Steps Consortium (2017)¹⁴

Ao finalizar a aplicação dos domínios, deve-se proceder a avaliação global da diretriz, a qual inclui a classificação da sua qualidade geral e a determinação se a mesma pode ser recomendada para o uso na prática clínica¹⁴. Segundo um estudo Japonês que avaliou a relação entre os itens que constituem os domínios do AGREE II e a avaliação geral das diretrizes utilizando regressão logística, os domínios “Rigor de desenvolvimento”, “Clareza da apresentação”, “Aplicabilidade” e “Independência editorial” exercem maior influência na avaliação da qualidade global da diretriz¹⁵.

Na literatura observa-se ascensão de estudos avaliando a qualidade de diretrizes clínicas. Revisões sistemáticas com aplicação do AGREE II estão disponíveis sobre temas

como: asma¹⁶, atividade física e movimentos seguros em osteoporose¹⁷, doença renal crônica distúrbios minerais e ósseos¹⁸, manejo de febre em crianças¹⁹, manejo farmacológico de doenças crônicas na atenção primária à saúde²⁰, diabetes mellitus²¹, bem como reabilitação após reconstrução de ligamento cruzado anterior²². É comum entre essas publicações os baixos escores atribuídos para os domínios “Envolvimento das partes interessadas”, “Rigor de desenvolvimento” e “Aplicabilidade”; sendo o último, em geral, o qual apresenta as menores pontuações em comparação aos demais critérios que compõe o AGREE II. Especificamente, em relação ao domínio rigor do desenvolvimento metodológico, o mesmo é crucial para que possam ser estabelecidas recomendações baseadas em evidências, sendo considerado critério chave para determinar a recomendação ou não da diretriz para uso na prática clínica¹⁸⁻²⁰. Já em relação à aplicabilidade das diretrizes, este domínio é frequentemente negligenciado durante o desenvolvimento da diretriz. Ou seja, não são apresentadas possíveis barreiras e facilitadores para sua aplicação, ferramentas para implementação da diretriz, implicação de recursos financeiros, bem como critérios para seu monitoramento²¹.

Nuckols e colaboradores avaliaram a aceitabilidade clínica de diretrizes com excelente rigor metodológico e qualidade técnica, sendo quatro das cinco analisadas classificadas como sendo moderadamente compreensíveis e válidas. Os autores concluíram que apesar de alto escore na qualidade global e especialmente no domínio rigor metodológico as diretrizes apresentam muito conteúdo de validade incerta e sugeriram que a aceitabilidade dos mesmos deveria ser independentemente avaliada previamente a sua disseminação. Tais resultados apontam que a alta qualidade metodológica de diretrizes não é suficiente para garantir que suas recomendações sejam de ótima qualidade, ou seja, clinicamente confiáveis e aplicáveis²³. A fim de preencher essa lacuna na avaliação de diretrizes, foi proposto o *Appraisal of Guidelines REsearch and Evaluation – Recommendations EXcellence* (AGREE-REX)¹¹. O AGREE-REX é um complemento ao AGREE II que engloba três domínios e foca especificamente na avaliação da qualidade das recomendações da diretriz, bem como, as justificativas que as sustentam. Estes domínios são compostos por um total de nove itens-chave seguidos de dois itens de classificação e avaliação global, os quais estão apresentados na **Tabela 2**²⁴. Os nove itens chave, bem como a orientação de como aplicar a ferramenta AGREE-REX podem ser consultados no website do AGREE, pelo link <https://www.agreetrust.org/resource-centre/agree-rex-recommendation-excellence/>.

Tabela 2 – Descrição dos domínios e itens que compõe o AGREE- REX

Domínio	Itens	Descrição
1) Aplicabilidade clínica	1-3	Diz respeito à evidência e aplicabilidade para utilizadores alvo, bem como população-alvo
2) Valores e preferências	4-7	Foca em valores e preferências dos utilizadores alvo, população alvo e desenvolvedores das recomendações de diretrizes
3) Implementabilidade	8-9	Diz respeito ao propósito das recomendações e aplicação local das recomendações propostas pela diretriz

Fonte: Adaptada de AGREE-REX Research Team (2019)²⁴

O AGREE-REX pode ser utilizado como método de avaliação da qualidade das recomendações (podendo ser aplicada para uma única recomendação, para um conjunto de recomendações ou para todas as recomendações da diretriz), bem como para auxiliar o desenvolvimento e relato das recomendações. Igualmente ao AGREE-II, ao finalizar a aplicação dos domínios, deve-se proceder a avaliação global das recomendações e definir se o conjunto de recomendações da diretriz é recomendado ou não para aplicação na prática clínica²⁴. Até o presente momento, o número de publicações utilizando o AGREE-REX ainda é escasso; porém observa-se que os níveis de evidência nos quais muitas das recomendações de diretrizes são baseadas são baixos, e os parâmetros do instrumento não são suficientemente esclarecidos nas diretrizes, o que possivelmente explica as baixas classificações nos seus domínios²⁵⁻²⁷.

3.2.1 Diretrizes clínicas para cuidado nutricional do paciente crítico

Idealmente, diretrizes acerca das etapas de sistematização do cuidado nutricional, devem seguir um rigor metodológico para dar suporte à prática baseada em evidência, a qual segue três princípios fundamentais: escolha das melhores evidências disponíveis, experiência clínica e valores e preferências dos pacientes^{7,28}.

Diversas sociedades de especialistas em terapia nutricional no paciente crítico de países distintos têm publicado diretrizes específicas. Nos últimos 13 anos as seguintes diretrizes foram publicadas por suas respectivas sociedades:

- 1) *Guidelines for specialized nutritional and metabolic support in the critically-ill patient – Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMICYUC-SENPE)*²⁹;
- 2) *Canadian Clinical Practice Guidelines*³⁰;
- 3) *Clinical Nutrition in Critical Care Medicine – German Society for Nutritional Medicine (DGEM)*³¹;
- 4) *Guidelines for nutrition support in critically ill patient – Société française d'anesthésie et de réanimation (SFAR)*³²;
- 5) *Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient – Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN)*³³;
- 6) *Early enteral nutrition in critically ill patients – European Society of Intensive Care Medicine (ESICM)*³⁴;
- 7) *ESPEN guideline on clinical nutrition in the intensive care unit – European Society for Clinical Nutrition and Metabolism (ESPEN)*³⁵;
- 8) *Diretriz Brasileira de Terapia Nutricional no Paciente Grave – Sociedade Brasileira de Nutrição Enteral e Parenteral (BRASPEN)*³⁶;
- 9) *Critical Illness Guideline – Academy of Nutrition and Dietetics (AND)*³⁷.

A qualidade de parte dessas diretrizes foi avaliada previamente por Fuentes Padilha e colaboradores, os quais publicaram em 2016 uma revisão sistemática de nove diretrizes para manejo nutricional do paciente grave. De acordo com a avaliação da qualidade das mesmas a partir da ferramenta AGREE II, foi observada uma qualidade global subótima, sendo somente quatro diretrizes recomendadas para utilização na prática clínica e classificadas como de alta qualidade: *ESPEN Guidelines on Enteral Nutrition: Intensive care* (2006), *Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: SCCM e ASPEN* (2016), *Critical Illness. Evidence-Based Nutrition Practice Guideline: AND* (2012) e *Canadian Critical Care Nutrition. Clinical Practice Guideline* (2015). Dentre as diretrizes avaliadas, os domínios com maiores escores foram “escopo e finalidade” e “clareza da apresentação” com pontuações de $76,2\% \pm 13,7\%$ e $76,9\% \pm 13,7\%$, respectivamente. Já os domínios com menores escores foram “aplicabilidade” e “independência editorial” com escores de $30,1\% \pm 22,8\%$ e $42,1\% \pm 23,9\%$. O escore médio do domínio “rigor de desenvolvimento” foi de $57,9\% \pm 18,1\%$, o que demonstra possíveis falhas em identificar e sintetizar as evidências, nos processos utilizados para a formulação de recomendações e na descrição dos planos de atualização da diretriz³⁸.

Cabe ressaltar que baixa qualidade das diretrizes pode também ser consequência de evidências científicas inadequadas e/ou conflitantes³⁹. De fato, um estudo com o objetivo de avaliar a qualidade de duas conhecidas diretrizes para a prática clínica do cuidado nutricional do paciente crítico (ASPEN/SCCM 2016 e ESPEN 2018) demonstrou que as recomendações de ambas eram em sua maioria apoiadas por opinião de especialistas⁴⁰. Isso pode ser atribuído ao fato de os estudos primários ainda apresentarem tamanho de amostra limitado, pela variabilidade da gravidade da doença, pela não identificação do estado nutricional no início do estudo e pelo poder insuficiente para análise estatística³³. O fato de uma minoria destas recomendações ser suportada por evidências de alta qualidade, reforça a necessidade de ensaios clínicos bem delineados para responder às questões de pesquisa que geram recomendações⁴⁰.

Cabe atentar também para o tempo entre a atualização da busca por evidências e a publicação das diretrizes⁴¹. Em pelo menos três diretrizes destinadas à terapia nutricional do paciente crítico há uma lacuna de até dois anos entre a busca pela evidência disponível e o momento em que a diretriz foi publicada³³⁻³⁵. Ademais, diretrizes de prática clínica comumente são utilizadas como “regras” por profissionais de saúde, porém recomendações enviesadas e/ou divergentes causam dilemas para esses profissionais na determinação de condutas³⁹. Ainda, é possível perceber uma falta de padronização das recomendações entre as diretrizes, o que implica em condutas heterogêneas, ou seja, gera distinções importantes entre as recomendações e tomada de decisões por parte dos profissionais nas UTIs o que pode levar a consequências deletérias para o paciente⁴².

3.2.1.1 Recomendações Nutricionais para Paciente Crítico

As principais semelhanças e divergências nas recomendações disponíveis nas diretrizes para manejo nutricional de paciente críticos acerca da sistematização do cuidado nutricional serão sumarizadas nos próximos parágrafos, considerando-se as etapas do cuidado nutricional.

Como primeira etapa do cuidado nutricional, quatro diretrizes recomendam a realização de triagem nutricional, sendo que ASPEN/SCCM e BRASPEN recomendam utilização de ferramentas como *Nutrition Risk in the Critically ill* (NUTRIC) ou *Nutritional Risk Screening* (NRS-2002)^{33,36} enquanto a ESPEN e SFAR consideram que todo paciente internado por mais de 48h em UTI deve ser considerado como em risco nutricional^{32,35}.

A realização de avaliação nutricional, segunda etapa do cuidado nutricional para que o diagnóstico nutricional possa ser firmado, é recomendada por sete diretrizes, sendo que os métodos para sua realização incluem: avaliação nutricional completa^{33,34,37}, Avaliação Subjetiva Global (ASG)^{29,31} e perda de peso^{29,32}.

No que diz respeito a etapa de intervenção nutricional, é consenso entre as diretrizes que o padrão ouro para determinação de necessidade energética é a utilização de calorimetria indireta. Todavia, por sua baixa disponibilidade na prática clínica, cinco diretrizes recomendam a utilização de equações preditivas como Penn-State^{29,37} e método de VCO₂^{31,35} ou fórmulas de bolso^{30,31-33,35,36}. Em relação ao aporte proteico, a maioria das diretrizes recomenda uma dieta hiperproteica, variando de 1,0-1,2g/kg/dia³¹ até 1,5-2,0g/kg/dia³⁶.

Desde que o paciente esteja em condições hemodinâmicas, recomenda-se a oferta de terapia nutricional precoce. Ou seja, é consenso entre as principais sociedades que a nutrição seja iniciada em até 48h após a admissão na UTI. Considerando a importância do início precoce da TN, deve-se definir qual a via de alimentação a ser adotada, dessa forma seis diretrizes recomendam a utilização de sonda em posição gástrica^{29,31-33,34,36}, sendo a posição pós-pilórica reservada para casos de alto risco de intolerância ou aspiração. Das nove diretrizes identificadas a literatura, somente três recomendam o uso de fórmula enteral polimérica padrão (isenta de fibras) para terapia nutricional no paciente crítico^{30,31-33}. Em casos de intolerância à nutrição enteral, somente três diretrizes fornecem informações sobre como esta condição deve ser monitorada. E, embora seja uma prática comum em diversas UTIs, a ASPEN/SCCM³³ e BRASPEN³⁶ recomendam que o monitoramento do volume residual gástrico não seja uma prática de rotina. Em relação à indicação de nutrição parenteral, cinco diretrizes fornecem orientações claras de quais condições indicam seu uso^{30,31,33,35,36}, contudo quando o início da terapia nutricional enteral não é bem tolerado não há consenso entre as entidades internacionais sobre em que momento se deve iniciar a nutrição parenteral.

As diretrizes também sumarizam etapas do cuidado nutricional relacionados à intervenção nutricional situações clínicas específicas. Nos casos de diarreia persistente a oferta de nutrição enteral não deve ser automaticamente interrompida até a investigação de sua etiologia^{33,36}, sendo que DGEM³¹ recomenda sua descontinuação somente em casos de diarreia refratária a outras alternativas de tratamento. Para pacientes com insuficiência renal em tratamento dialítico, quatro^{29,32,33,36} das nove diretrizes recomendam o aumento do aporte proteico de 1,5g/kg/dia³⁶ até um máximo de 2,5g/kg/dia^{29,33,36}. Como nos pacientes críticos gerais, aqueles com pancreatite aguda severa também devem receber terapia nutricional

precoce^{29,33-35}. ASPEN/SCCM³³ e BRASPEN³⁶ ressaltam que não há diferença entre oferta de nutrição enteral via sonda nasoentérica em posição gástrica ou jejunal para estes pacientes. Sendo a nutrição parenteral recomendada somente na impossibilidade de oferta nutricional por via enteral^{29,33,36}, com indicação de início após uma semana do episódio de pancreatite^{33,36}.

Nos casos de pacientes sépticos, a maioria das diretrizes não traz recomendações acerca desta condição clínica. Duas diretrizes recomendam o início de terapia nutricional precoce após estabilização clínica^{33,35}, e a utilização de fórmulas especializadas é controversa^{29,32}. Em pacientes com falência hepática na etapa de avaliação antropométrica a utilização do peso seco ou usual é recomendada^{33,36}. Em relação à terapia nutricional, nestes pacientes não é recomendado por três diretrizes a utilização de aminoácidos de cadeia ramificada^{29,33,36}. As sociedades SEMICYUC-SENPE²⁹, Canadense³⁰ e AND³⁷ indicam o uso de fórmula imunomoduladoras para pacientes com falência pulmonar, enquanto a BRASPEN³⁶ não recomenda a utilização de fórmulas com ômega-3 e antioxidantes. Por fim, em relação ao paciente crítico obeso seis das nove diretrizes orientam condutas específicas para essa situação. É consenso a utilização de calorimetria indireta para estimativa de gasto energético e oferta de nutrição hipocalórica^{29,31,33,35-37}, bem como oferta de alto aporte proteico variando de 1,8g/kg/dia^{29,31} até 2,5g/kg/dia^{29,33,36} do peso ideal ou 1,3g/kg/dia do peso ajustado³⁵.

Na **Tabela 3** estão sumarizadas as recomendações das diferentes etapas do cuidado nutricional do paciente crítico compiladas nas diretrizes clínicas publicadas nos últimos cinco anos. Essa restrição justifica-se pela constante atualização de condutas nutricionais no manejo do paciente crítico.

Tabela 3 - Recomendações para o cuidado nutricional do paciente crítico nas diretrizes clínicas publicadas nos últimos cinco anos

Recomendação	SCCM/ASPEN, 2016 ³³	ESICM, 2017 ³⁴	BRASPEN, 2018 ³⁶	ESPEN, 2019 ³⁵	DGEM, 2019 ³¹
Triagem Nutricional	NRS-2002 ou NUTRIC podem ser utilizados em todos os pacientes admitidos em UTI	ND	Risco nutricional deve ser avaliado em paciente críticos (os autores comentam que a NRS-2002 ou NUTRIC score podem ser aplicáveis)	Todo paciente crítico com internação em UTI > 48h pode ser considerado como em risco de desnutrição	ND (Autores comentam que todos os pacientes admitidos em UTI tem alto risco nutricional)
Avaliação Nutricional	Avaliação de comorbidades, função do TGI e risco de aspiração	ND	ND (Autores comentam que a avaliação nutricional é uma boa estratégia para identificar de forma precoce e tratar a desnutrição)	Anamnese, relato de perda de peso não intencional ou diminuição do desempenho físico, exame físico, composição corporal e massa e força muscular, se possível.	Podem ser usados critérios para diagnóstico de desnutrição específicos para doença propostos pelo DGEM ou ASG
Intervenção nutricional: Necessidade de energia	1ª opção: CI 2ª opção: equações preditivas ou 25–30 kcal/kg/dia	ND	1ª opção: CI 2ª opção: 15-20 kcal/kg/dia e progressão para 25-30 kcal/kg/dia após o quarto dia da recuperação do paciente	1ª opção: CI 2ª opção: VO2 do cateter da artéria pulmonar ou VCO2 derivado do ventilador mecânico (Requerimento Energético = VCO2 x 8,19). 3ª opção: 20-25 kcal/kg/dia.	1ª opção: CI 2ª opção: VCO2 derivado do ventilador mecânico (REE = VCO2 x 8,19) 3ª opção: em pacientes críticos não obesos 24kcal/kg peso atual/dia.
Intervenção nutricional: Aporte proteico	1,5-2,0 g/kg/dia	ND	1,5-2,0 g/kg/dia	1,3 g/kg/dia	1,0-1,2 g/kg peso atual/ dia
Intervenção nutricional: Início da terapia nutricional	NE precoce nas primeiras 24–48h quando os pacientes são incapazes de manter ingestão voluntária	NE precoce nas primeiras 48h de internação	NE precoce nas primeiras 24–48h quando os pacientes são incapazes de receber nutrição oral.	Se a nutrição VO não for possível, iniciar NE precoce nas primeiras 48h de internação.	Primeiras 24 h após admissão na UTI nos pacientes com incapacidade de manter ingestão voluntária durante a fase aguda da doença crítica.

Tabela 3 - Continuação

Recomendação	SCCM/ASPEN, 2016 ³³	ESICM, 2017 ³⁴	BRASPEN, 2018 ³⁶	ESPEN, 2019 ³⁵	DGEM, 2019 ³¹
Intervenção nutricional: rota para alimentação	NE antes de NP.	NE antes de NP.	NE antes de NP.	Preferir dieta VO antes de NE e NP nos pacientes capazes de alimentar-se. Se VO não for factível, NE deve ser iniciada antes de NP.	NE na incapacidade de manter ingestão voluntária.
Intervenção nutricional: Posição da sonda	Acesso gástrico Acesso pós-pilórico deve ser utilizado em pacientes com alto risco de aspiração.	ND	Acesso pós-pilórico deve ser utilizado em pacientes com alto risco de aspiração e naqueles com intolerância GI.	Acesso gástrico como padrão. Acesso pós-pilórico deve ser utilizado em pacientes com alto risco de aspiração, naqueles com intolerância do TGI não resolvida com agentes pró cinéticos.	Acesso gástrico deve ser preferido à via de acesso jejunal, exceto quando o risco de aspiração/ volume residual gástrico for alto.
Intervenção nutricional: Tipo de fórmula enteral	Fórmula enteral padrão polimérica. Deve-se evitar uso de fórmulas especializadas.	ND	ND	ND	Fórmulas contendo fibras não devem ser utilizadas na fase aguda quando há alto risco de isquemia mesentérica.
Intervenção nutricional: Indicação de NP	Quando NE não é viável, NP exclusiva deve ser iniciada o mais rápido possível em pacientes com alto RN ou gravemente desnutridos. Em pacientes com baixo RN, NP exclusiva deve ser iniciada após os primeiros 7 dias de internação na UTI se a ingestão voluntária não puder ser mantida e se a NE precoce não for viável.	ND	Em pacientes com alto RN na admissão e que não puderem usar o TGI, a NP deve ser iniciada o mais rápido possível.	NP precoce e progressiva pode ser fornecida em caso de contraindicações de NE em pacientes gravemente desnutridos. Em caso de contraindicações para VO e NE, a NP deve ser implementada dentro de três a sete dias	Se houver contraindicações para oferta de NE, a PN deve ser iniciada.

Tabela 3 - Continuação

Recomendação	SCCM/ASPEN, 2016 ³³	ESICM, 2017 ³⁴	BRASPEN, 2018 ³⁶	ESPEN, 2019 ³⁵	DGEM, 2019 ³¹
Monitorando a intervenção nutricional	A tolerância à NE deve ser monitorada diariamente e a interrupção inadequada da NE e pedidos de NPO devem ser evitados. VRG não deve ser usado como parte dos cuidados de rotina para monitorar tolerância à NE	ND	A mensuração de VRG não deve ser usada rotineiramente em pacientes críticos.	ND	ND
Situações específicas: Diarreia	NE não deve ser interrompida automaticamente em casos de diarreia. Fórmulas com pequenos peptídeos ou fórmula comercial contendo mix de fibras devem ser usadas em caso de diarreia persistente.	NE precoce deve ser utilizada com pacientes críticos mesmo na presença de diarreia.	NE não deve ser interrompida automaticamente em casos de diarreia. O uso de fibras solúveis deve ser considerado.	ND	Suspender NE somente em casos de diarreia refratária.
Situações específicas: Terapia de substituição renal	Não restringir oferta de proteína como forma de evitar ou adiar o início da hemodiálise. Oferta proteica máxima de 2,5 g/kg/dia.	ND	Oferta proteica de 1,5-2,5 g/kg/dia	ND	Ofertar mesma quantidade de proteína que pacientes não realizado hemodiálise
Situações específicas: Pancreatite aguda grave	NE trófica deve ser iniciada. O uso de NE sobre NP é indicado. NE deve ser fornecida ao paciente por via gástrica ou jejunal. NP deve ser considerada após 1 semana do início do episódio de pancreatite.	Utilizar NE precoce	Usar NP quando não atingir 60% do requerimento nutricional após 7 dias de NE, exceto em pacientes desnutridos. Não há diferença entre a posição gástrica ou jejunal do tubo enteral para a tolerância do TGI.	Utilizar NE precoce	ND

Tabela 3 - Continuação

Recomendação	SCCM/ASPEN, 2016³³	ESICM, 2017³⁴	BRASPEN, 2018³⁶	ESPEN, 2019³⁵	DGEM, 2019³¹
Situações específicas: Sepse	NE deve ser iniciada dentro de 24–48h, assim que a ressuscitação for concluída e o paciente estiver estável. Não usar NP exclusiva ou suplementar a NE. Nutrição trófica (10–20 kcal/h ou até 500 kcal/dia) na fase inicial da sepse, avançando após 24–48 horas para >80% do requerimento energético.	ND	ND	NE precoce e progressiva deve ser usada após a estabilização. Se contraindicada, NE deve ser substituída por PN	ND
Situações específicas: Falência hepática	Utilizar peso seco ou usual. Não há evidência para uso de fórmulas com BCAA em pacientes com encefalopatia que já estão recebendo terapia de primeira linha com antibióticos de ação luminosa e lactulose.	NE trófica deve ser iniciada em pacientes com insuficiência hepática aguda.	Utilizar peso usual. Preferir NE, NP deve ser uma opção quando as necessidades de NE não são atendidas. Não é recomendável a utilização de BCAA.	NE trófica deve ser iniciada em pacientes com insuficiência hepática aguda.	ND
Situações específicas: Falência pulmonar	Não utilizar fórmulas com alto teor de gordura/ baixo teor de carboidratos para manipular o quociente respiratório e reduzir o CO ₂ .	ND	Não são indicadas fórmulas enterais com ômega-3 e antioxidantes. É indicado o uso de fórmulas enterais de alta densidade.	ND	ND

Tabela 3 - Continuação

Recomendação	SCCM/ASPEN, 2016³³	ESICM, 2017³⁴	BRASPEN, 2018³⁶	ESPEN, 2019³⁵	DGEM, 2019³¹
Situações específicas: Obesidade	Oferta hipocalórica e hiperproteica. Utilizar fórmula enteral com baixa densidade calórica (1kcal/mL) e NPC:N reduzido. Não exceder 65-70% do requerimento energético aferido por CI. Na indisponibilidade de CI: IMC entre 30-50kg/m² oferta de 11-14kcal/kg peso atual/dia e IMC >50 oferta de 22-25 kcal/kg peso ideal/dia Oferta proteica: se IMC 30-40kg/m² oferta de 2,0 g/kg peso ideal/dia ou IMC >40 oferta de 2,5g/kg peso ideal/dia.	ND	Utilizar fórmulas de baixa densidade, hiperproteica, sem imunonutrientes, com redução da relação NPC:N. Não exceder 65-70% do requerimento energético aferido por CI. Na indisponibilidade de CI: IMC 30-50kg/m² oferta de 11-14kcal/kg peso atual/dia e IMC >50 oferta de 22-25kcal/kg peso ideal/dia. Oferta proteica: IMC 30-40kg/m² oferta de 2,0g/kg peso ideal/dia ou IMC >40 oferta de 2,5g/kg peso ideal/dia.	Fornecer dieta isocalórica hiperproteica, guiada por CI e perdas urinárias de nitrogênio. Na indisponibilidade de CI, basear a necessidade energética no peso atual ajustado. Oferta proteica: guiada pelas perdas de nitrogênio urinário ou massa corporal magra, e na indisponibilidade a ingestão pode ser de 1,3g/kg peso ajustado/dia.	Utilizar CI para estimativa de necessidades energéticas. Ofertar 60% da estimativa de requerimento energético ou 11-14 kcal/kg peso atual/dia se IMC entre 30-50 kg/m² ou 22-25 kcal/kg peso ideal/dia se IMC >50 kg/m². Oferta proteica: se IMC >30kg/m² oferta de 1,5g de proteína (ou 1,8 g de aminoácidos)/kg de peso ideal/dia.

Legenda: Academy of Nutrition and Dietetics (AND); American Society for Parenteral and Enteral Nutrition (ASPEN); Aminoácidos de Cadeia Ramificada (BCAA); Avaliação Subjetiva Global (ASG), Calorimetria Indireta (CI); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society of Intensive Care Medicine (ESICM); German Society for Nutritional Medicine (DGEM); Índice de Massa Corporal (IMC); Nada Por Via Oral (NPO); Não Descrito (ND); Nutrição Enteral (NE); Nutrição Parenteral (NP); Nutrition Risk in the Critically ill (NUTRIC); Nutritional Risk Screening (NRS-2002); Risco Nutricional (RN); Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC); Sociedad Española de Nutrición Parenteral y Enteral (SENPE); Sociedade Brasileira de Nutrição Parenteral e Enteral (BRASPEN); Société française d'anesthésie et de réanimation (SFAR); Society of Critical Care Medicine (SCCM); Trato Gastrointestinal (TGI); Unidade de Terapia Intensiva (UTI); Via Oral (VO); Volume Residual Gástrico (VRG).

Além de possíveis vieses e falta de padronização de recomendações, a população de pacientes críticos é heterogênea, o que também reduz a validade externa das recomendações. Esse fato deve ser considerado como base para apoiar a tomada de decisões⁴³. Todavia, sabe-se que a adesão às diretrizes clínicas pode melhorar o desfecho clínico do paciente. Uma revisão sistemática com o objetivo de avaliar as evidências para a eficácia da implementação de diretrizes clínicas holandesas identificou que dentre os 19 estudos que avaliaram o impacto das diretrizes na qualidade do cuidado 17 demonstraram melhorias na estrutura e processo de cuidado. Ademais, dos nove estudos que avaliaram o impacto da implementação das recomendações de diretrizes nos desfechos dos pacientes, seis deles demonstraram melhorias em pelo menos um dos desfechos avaliados⁴⁴. Contudo, revisão sistemática com o objetivo de avaliar a extensão da adesão às diretrizes para manejo de síndromes coronárias agudas, demonstrou grande variação (menos de 5% a mais de 95%) nas taxas de adesão às recomendações das diretrizes. Esse fato, possivelmente reflete lacunas na prática clínica baseada em evidência⁴⁵. Os estudos mostraram que, apesar dos benefícios importantes e da influência positiva das diretrizes de terapia nutricional nas práticas nutricionais e no curso clínico da doença crítica, existem fatores que dificultam sua implementação. Alguns exemplos são: custos elevados para treinamento dos profissionais para sua implementação, ausência de algoritmos como uma versão “operacional” da diretriz a fim de facilitar sua aplicação prática, ausência de equipe multidisciplinar e nutricionista em tempo integral na UTI, diretrizes com declarações vagas ou complexas, numerosas diretrizes conflitantes sobre o mesmo tema - o que leva a falta de consenso sobre quais diretrizes adotar^{46,47}. Dessa forma recomenda-se mais estudos direcionados para avaliação da qualidade de diretrizes e suas recomendações para a viabilidade e o desenvolvimento de estratégias ou modelos de implementação na prática clínica⁴².

3.2.2 Qualidade das diretrizes clínicas para cuidado nutricional de pacientes com outras patologias

Além da avaliação da qualidade de diretrizes clínicas de cuidado nutricional para o paciente crítico conforme mencionado no item 3.2.1, outras revisões sistemáticas utilizando o instrumento AGREE II foram conduzidas voltadas a pacientes queimados graves, oncológicos e com doença renal crônica.

Grammatikopoulou e colaboradores identificaram oito diretrizes para manejo nutricional de pacientes queimados graves com uma qualidade geral que variou de 29,2% a 100%, e rigor metodológico inferior a 50% na maioria das diretrizes avaliadas. Consequentemente, somente uma diretriz atingiu pontuações suficientes para ser recomendada sem modificações. Os autores destacam que a qualidade geral inadequada apresentada pelas diretrizes, é um fator importante a ser considerado para melhorias metodológicas no desenvolvimento de futuras diretrizes⁴⁸.

De forma semelhante, Zhao e colaboradores avaliaram a qualidade de diretrizes de cuidados nutricionais para pacientes com câncer, bem como buscaram identificar lacunas que limitam a prática baseada em evidências. Dezesete diretrizes foram incluídas, e qualidade global que variou de 24,4% a 94,5% foi observada. No domínio rigor de desenvolvimento a maior parte das diretrizes apresentou pontuação inferior a 60%. Sendo assim, somente duas diretrizes foram fortemente recomendadas, enquanto onze foram recomendadas com modificações e quatro não recomendadas. Ademais, as recomendações geradas pelas diretrizes apresentaram importante variação, o que implica em uma limitada prática baseada em evidências⁴⁹.

Com a ascensão de publicações de diretrizes de prática clínica em relação ao manejo nutricional de pacientes com doença renal crônica, recentemente Bakaloudi e colaboradores, conduziram uma revisão sistemática com o objetivo de avaliar a qualidade destas diretrizes e fornecer recomendações para futuras atualizações. Onze diretrizes foram identificadas e nenhuma apresentou um limiar de alta qualidade, sendo três classificadas com moderada qualidade e recomendada com modificações e as oito restantes não recomendadas. Esse resultado, segundo os autores, reflete uma má descrição das informações relevantes na diretriz ou sua total ausência. Com base nos itens que compõe o AGREE II, existem vários campos na qualidade das diretrizes que podem ser melhorados. Em um deles, rigor de desenvolvimento, a intensa heterogeneidade encontrada entre as pontuações comprovam a existência de lacunas significativas em relação às diretrizes no seu desenvolvimento metodológico⁵⁰.

4 JUSTIFICATIVA

A terapia nutricional no paciente crítico tornou-se um importante componente do manejo clínico deste paciente, não sendo mais somente uma terapia adjuvante, mas uma estratégia para atenuar a resposta ao estresse e modular a resposta imune com potencial impacto nos desfechos clínicos do paciente^{33,42}. Dessa forma, a avaliação da qualidade metodológica das diretrizes de cuidado nutricional para paciente crítico é crucial no intuito de fornecer informações valiosas para tomada de decisões baseadas em evidências, bem como futuro desenvolvimento de novas diretrizes mais rigorosas e de alta qualidade. Nos últimos cinco anos, após a publicação da revisão sistemática conduzida por Fuentes Padilla e colaboradores³⁸, pelo menos quatro novas diretrizes foram publicadas^{31,34,35,36}, o que justifica sua atualização. Além disso, não identificamos na literatura uma revisão sistemática que tenha aplicado o AGREE-REX para avaliação da qualidade das recomendações das diretrizes de prática clínica de cuidado nutricional para pacientes adultos críticos.

5 OBJETIVOS

5.1 OBJETIVO GERAL

Avaliar criticamente a qualidade metodológica e das recomendações de diretrizes de prática clínica para o cuidado nutricional de pacientes adultos críticos e investigar o grau de concordância entre suas recomendações.

5.1.1 Objetivos específicos

- a) avaliar criticamente a metodologia de diretrizes de prática clínica para o cuidado nutricional de pacientes adultos críticos utilizando o instrumento AGREE II;
- b) avaliar criticamente a qualidade das recomendações de diretrizes de prática clínica para o cuidado nutricional de pacientes adultos críticos utilizando o instrumento AGREE-REX;
- c) avaliar a frequência de concordância das recomendações de diretrizes de prática clínica para o cuidado nutricional de pacientes adultos críticos.

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7 ARTIGO

Quality appraisal of clinical nutrition practice guidelines for critically ill adult patients: A systematic review using the AGREE II and AGREE-REX tools

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ABSTRACT

Purpose: Nutritional therapy should follow evidence-based practice, thus several societies regarding nutrition and critical care have developed specific Clinical Practice Guidelines (CPG). However, to be regarded as trustworthy the quality of the CPG for critically ill patients and its recommendations need to be high. This systematic review aimed to appraise the methodology and recommendations of nutrition CPGs for critically ill patients, and investigate the degree of agreement between their recommendations.

Methods: A systematic review was performed (protocol number CRD42020184199), and the search on Pubmed, Embase, Cochrane Library, and other four specific databases of guidelines was conducted up to June 2021. Two reviewers independently, assessed titles and abstracts and potentially eligible full text reports to determine eligibility and subsequently four reviewers appraised the guidelines quality using the Advancing Guideline Development, Reporting and Evaluation in Health Care instrument II (AGREE-II) and AGREE-Recommendation Excellence (AGREE-REX). The frequency of agreement between CPGs recommendations was calculated.

Results: Nine CPG for nutrition in critically ill patients were identified. Only Academy of Nutrition and Dietetics and European Society of Intensive Care Medicine had a total acceptable quality and were recommended for daily practice according AGREE-II. None of the CPG recommendations had an overall quality score above 70%, thus being classified as moderate quality according AGREE-REX. The major recommendations for each step of nutrition care process for critically ill patients were based on expert consensus, and the agreement between CPGs were $\leq 50\%$ for the most of them.

Conclusion: The methodological evaluation of the critically ill adult patient CPGs revealed significant discrepancies and showed a need for improvement in its development and/or reporting. In addition, recommendations about nutrition care process varied greatly across CPG, and were most based in consensus statements.

Keywords: Critical care; Intensive care unit; Practice guidelines; Nutrition therapy; Health Care Quality Assessment.

INTRODUCTION

Critical illness is associated with intense catabolism that is driven by a systemic inflammatory response that is coupled with complications of increased resting energy expenditure, negative nitrogen balance, and progressive reduction in fat and muscle mass, leading to worse clinical outcomes, such as increased infection, multiple-organ dysfunction, longer length of stay, and mortality [1]. Nutrition therapy in this scenario represents not only adjuvant care, but also a strategy to reduce the metabolic response to stress, prevent oxidative cellular injury, and positively modulate immune responses. Individualized nutritional interventions through early enteral feeding, appropriate nutrient delivery regimens, and glycemic control can improve the clinical course of critical illness, and should be the basis for efficient therapy that impacts patient outcomes [2].

Nutritional therapy should follow evidence-based practice and involves three fundamental principles: awareness of the best available evidence, clinical experience, and patient values and preferences [3]. In this sense, rigorously developed clinical practice guidelines (CPGs) provide support to healthcare professionals by establishing standards across the healthcare continuum (including screening and diagnosis), supported by the strongest scientific evidence available [4]. The development of high-quality CPGs is a challenging task, and for it to be trustworthy, it should: a) be based on a systematic review; b) be developed by a multidisciplinary expert workgroup and representatives of intended users; c) consider target population views and preferences; d) be based on an explicit and transparent process that minimizes distortions, biases, and conflicts of interest; e) provide a clear explanation of evidence syntheses, consider health benefits, side effects, and risks to formulate the recommendations; f) rate the quality of evidence and the strength of the recommendations; g) present a procedure for updating the guidelines when important new evidence warrants modification of the recommendations [4].

The AGREE collaboration defines guideline quality as “confidence that the potential biases inherent in guideline development have been addressed adequately and that the recommendations are both internally and externally valid, and are feasible for practice” [6]. The Appraisal of Guidelines for Research & Evaluation II (AGREE II) is a validated and reliable tool specially designed to assess the issue of variability in guideline quality [5,6], through which many critical appraisals of guidelines have been

performed and published [7-9]. AGREE II has been shown to be the most widely used CPG assessment tool in a systematic review of 24 different tools [10]. Although meeting rigorous methodological requirements is necessary, it is not sufficient to ensure that guideline recommendations are clinically credible or implementable. Thus, AGREE-Recommendation Excellence (AGREE-REX) was proposed to address this gap and assess the quality of guideline recommendations, which is also used as a strategy to inform their development and reporting [11].

Several societies regarding nutrition and critical care in different countries have developed specific guidelines. A systematic review published in 2016 aimed to appraise the methodological quality of critically ill patients' CPGs using AGREE II, and demonstrated overall suboptimal CPG quality in this field, i.e. only four of nine CPGs were rated as "recommended." Major deficiencies were found in applicability, editorial independence, stakeholder involvement, and rigor of development domains [12]. A lack of globally standardized procedures implies a vastly heterogeneous clinical management of nutrition therapy in the intensive care setting. Biased and divergent recommendations between different guidelines can also create a dilemma for professionals who choose not to follow the recommendations they distrust [13].

In the last five years, at least four CPGs have been published [14-17] in which updated evaluations of the guidelines for the nutrition care of critically ill patients are needed. Moreover, to the best of our knowledge, there is no systematic review that has applied AGREE-REX to the clinical nutrition practice guidelines for critically ill adult patients. In order to provide valuable information for clinical practice and for the further development of CPGs, the current systematic review aimed to critically appraise the methodology and recommendations of clinical nutrition CPGs for critically ill patients published in the last 13 years. In addition, we investigated the degree of agreement between their recommendations from evidence to decision making.

METHODS

Design and registration

The current systematic review was conducted based on the Cochrane Handbook recommendations [18] and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [19]. The protocol of this

study was registered in the International Prospective Register of Systematic Reviews (identifier: CRD42020184199).

Eligibility criteria

The most up-to-date version of CPGs for critically ill adults that addressed recommendations for nutrition therapy were included if they: (1) employed a grading system to rate the quality of evidence; (2) were published in a peer-reviewed journal or in a guideline database; (3) were published in the last 13 years, the maximum period for updating the guidelines, and (4) were intended for health professionals and had included recommendations.

CPGs were excluded if they were exclusively dedicated to the pediatric patient population. We also excluded position or consensus statements, as well as commentaries that summarized the evidence from a published CPG and made recommendations according to local factors. CPGs with unavailable text were excluded.

Clinical practice guideline identification

The literature search to identify guidelines according to the inclusion criteria was performed in May 2020, and the last update was conducted on June 2021.

Search strategy

The current systematic review addresses three research questions:

1. What is the quality of the evidence-based nutrition practice guidelines for critically ill adult patients?
2. What is the quality of the recommendations of the evidence-based nutrition practice guidelines that meet a minimum methodological threshold of moderate and high quality in AGREE II?
3. What is the degree of agreement across the recommendations of the evidence-based nutrition practice guidelines?

It was constructed according to the “PICAR” framework — P: Population, clinical condition; I: Interventions, C: Comparator, A: Attributes of eligible CPGs, and R: Recommendation characteristics [20]; which are detailed in **Table 1**.

Search database

The search for CPGs was performed in PubMed, Embase, Cochrane Library, National Institute for Health and Clinical Excellence (NICE), National Guideline Clearinghouse - Agency of Healthcare Research and Quality (AHRQ), the Intercollegiate Guidelines Network (SIGN), and Guideline International Network (GIN) databases, with no restrictions on language or date of publication, using specific keywords according to each database.

Newly published articles were screened every month until the final version of the manuscript was submitted. The references of all eligible CPGs for additional relevant guidelines were screened, and a manual search was performed through other potentially relevant guideline databases, such as the American Society for Parenteral and Enteral Nutrition (ASPEN), European Society for Clinical Nutrition and Metabolism (ESPEN), Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismo (FELANPE), and Parenteral and Enteral Nutrition Society of Asia (PENSA).

The full electronic search strategy used in PubMed is presented in **Box 1**. The search strategy adopted for Embase and the Cochrane Library is available in **Online Supplements 1 and 2**.

Process of CPG selection and data extraction

The EndNote reference manager software program (version X7.17, New York City: Thomas Reuters, 2011) was used to coordinate the review and tracking process. Two trained reviewers independently screened the titles and abstracts (AC and PPT), and subsequently evaluated the full-text versions of all potentially relevant articles as well as the supporting materials of each included CPG. A third reviewer (FMS) resolved all cases of disagreement.

Data extraction was performed using Google Forms® and exported to Microsoft Office Excel®. It was guided by a standardized electronic form and independently performed by two reviewers (AC and PPT). Disagreements were discussed, analyzed, and resolved through the arbitration of a third reviewer (FMS). The characteristics extracted from each CPG included: journal, publication year, location, society, first author's name, first version of the guideline or its update, target audience, registered dietitian in the development team, methodology development, type of meta-analysis (direct, indirect only, or mixed evidence), and the grading system to rate the quality of

evidence. The main recommendations for nutrition care process steps were also extracted: nutrition risk screening, nutrition assessment and diagnosis, start of nutrition therapy (time, route, and dose), monitoring tolerance and adequacy of nutrition therapy, selection of appropriate enteral formulation, parenteral nutrition (PN), and nutritional therapy for specific clinical conditions. Authors were contacted in case of doubts regarding the methodology of the development of their CPG by mail at three different instances, and if they did not reply, the available information in the publication was considered.

Quality assessment of clinical practice guidelines and their recommendations

The English version of the most recent version of the AGREE II tool (2017) was employed to evaluate the quality of the CPGs. The tool comprises the following six domains: 1) scope and purpose, 2) stakeholder involvement, 3) rigor of development, 4) clarity and presentation, 5) applicability, and 6) editorial independence. The domains were then refined to 23 items in total, and each of them was rated on a 7-point agreement scale from 1 (strongly disagree) to 7 (strongly agree). In addition, an overall global quality assessment was assigned by the rater from 1 (lowest possible quality) to 7 (highest possible quality), with a final statement on whether to use the guideline in practice or not (“yes,” “yes with modifications,” or “no”) [21].

Each CPG was independently rated by four reviewers (AC, PPT, ICE, and FMS), who held degrees in clinical nutrition and had experience in performing systematic reviews and methodological evaluations of literature. All reviewers were trained to apply the AGREE II tool by studying its manual and performing the online training offered by the AGREE PLUS platform. Reviewers first read the full version of the CPGs and reviewed all relevant information regarding the guideline development process, including the supplementary material related to the CPG. Using two clinical guidelines [2,17], a pilot appraisal trial was performed in order to rehearse the experience of using AGREE II, and then the results were discussed. All reviewers were instructed to share relevant supplementary materials with the group to ensure that all reviewers could evaluate the same information.

The score for each domain was obtained by summing all the scores of each reviewer for all items in a domain, and then standardized as follows: (obtained score - minimum possible score)/(maximum possible score - minimum possible score) [21].

One reviewer summed all scores, and each domain score was calculated and presented in a table of results.

Considering that the AGREE II manual does not provide cut-off points for the interpretation of the scores, after the assessment of the 23 items and the comprehensive judgment by reviewers, the selected guidelines were evaluated by their quality, followed by the decision if the CPGs were to be recommended for use in clinical practice. For overall quality assessment, mean domain scores were categorized as good ($\geq 80\%$), acceptable (60%–79%), moderate (40%–59%), or low ($< 40\%$) [7,9]. With regard to these recommendations, the following criteria were considered: if four of the six domains were categorized as $\geq 60\%$, including domain 3 (rigor of development), the CPG was recommended; if at least two domain scores were categorized above 60%, the CPG was recommended with modifications; and if three of the six domain scores were categorized as less than 30% or none of the domains were above 60%, the CPG was not recommended [7].

As a complement to AGREE II, the AGREE-REX tool was used for quality evaluation of the CPG recommendations that meet a minimum methodological threshold of moderate and high quality in AGREE II. This tool comprises the following three domains: 1) clinical applicability, 2) values and preferences, and 3) implementability. The domains were then refined to nine items in total, and each of them was rated on a 7-point agreement scale from 1 (strongly disagree) to 7 (strongly agree) [11].

AGREE-REX was applied to a group of recommendations (steps of nutrition care processes) defined *a priori* by four independent reviewers (AC, PPT, ICE, and FMS) that also applied the AGREE II tool. The evaluations were performed independently and evaluators were blinded to the other evaluators' assessments. The scoring system for each domain was equal to that of AGREE II, as described previously. For overall quality assessment, the cutoff points suggested by the AGREE-REX manual were adopted: guidelines with overall scores $> 70\%$ were defined as high quality, those with overall quality scores $< 30\%$ as lower quality, and all others as moderate quality [11].

Data synthesis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS)

version 22.0. The means and standard deviations or medians and interquartile amplitudes (according to the domain distribution) were computed for the domain scores and overall scores. The normality of the domains was tested using the Shapiro Wilk test.

The inter-rater agreement was computed using the Intraclass correlation coefficient (ICC) with a two-way random effects model for each domain and total score. The level of agreement (ICC) was classified according to commonly cited cut-offs as follows: poor (<0.40), fair ($0.40\text{--}0.59$), good ($0.60\text{--}0.74$), or excellent ($0.75\text{--}1.00$) [22].

CPGs were grouped according to their AGREE II quality (acceptable, moderate, and low quality) in the two groups in order to investigate the possible features associated with high quality. Moderate and acceptable quality CPGs were grouped as the highest quality. Features were selected in accordance with prior studies [8-10]: year of publication, number of authors (grouped by median), type of institution (specialty society or governmental institution), region (developed or developing country), version (first version or updated version), reported funding, and method for development. A qualitative evaluation was performed owing to the reduced number of CPGs.

The frequency of concordance between the CPGs regarding the recommendations was calculated.

RESULTS

Selection and general characteristics of eligible CPGs

A total of 7358 articles were initially identified through database searches, of which 834 were duplicates. Additional records through manual search and review of gray literature amounted to five articles. **Figure 1** illustrates the flow of the guideline selection. The full texts of 24 articles were assessed for eligibility, and 18 of them were included in the current systematic review [2,14-17,23-35], which comprised nine CPGs for critically ill adults addressing recommendations for the nutrition care process. The guidelines for specialized nutritional and metabolic support in critically ill patients published by the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMICYUC-SENPE) comprised ten articles [23-32].

The CPGs included were published between 2012 and 2019 in six different countries, most of them in the United States (three CPGs) [2,14,35] and in the English

language (seven CPGs) [2,14,16,17,23-33,35]. Only the European Society of Intensive Care Medicine (ESICM) guideline [14] was an original version. Most CPGs reported funding [2,14,16,23-33,35], based their recommendations in meta-analyses [2,14-17,23-33,35], and used the GRADE system to grade their evidence [2,14,15,17,23-32,34]. In eight guidelines, the names of all authors had been described, and the mean number of authors was 16 (ranging from six [34] to 24 [14]). Seven CPGs listed the references used in its content. The mean number of CPG references was 329 (ranging from 75 [14] to 502 [16]). The general features of eligible CPGs are presented in **Table 2**.

Quality appraisal of CPGs

Table 3 presents the AGREE II quality scores for each of the nine CPGs included in the current review. The median overall quality of the CPGs was equal to 3.5 (SD = 1.4). None of the CPGs had an overall quality score above 80%, two CPGs scored between 60–79% [14,35], and five CPGs scored below 40% [15,16,23-34]. Only two CPGs achieved acceptable quality and were strongly recommended [14,35], while three were recommended with modifications [2,16,17], and four were not recommended for use in clinical practice [15,23-34]. **Online Supplement 3** presents the individual scoring of AGREE II for each CPG.

The domains with higher scores were the ‘clarity of presentation’ domain (domain 4), with a mean score of $80.2 \pm 11.2\%$, and the ‘editorial independence’ domain (domain 6), with a median score of 66.7%. The lowest score was in the ‘applicability’ domain (domain 5), with a median score of 7.3%.

The inter-rater reliability was excellent for the overall mean score (> 0.900), and it was higher than 0.750 for the majority of the domains. A description of the evaluation performed for each domain of AGREE II is presented below.

Domain 1: Scope and purpose

The AGREE II quality scores for domain 1 ranged from 13.9% to 83.3%, and the scores of the five CPGs were greater than 60% for this domain [14,16,17,33,35]. Low scores were given to four CPGs [2,15,23-32,34] due to lacks in providing detailed and adequate descriptions of overall objectives, health questions, and clarity as to which population the CPG was meant to be applied to.

Domain 2: Stakeholder involvement

The AGREE II quality scores of domain 2 ranged from 8.3% to 79.6%. The majority of the CPGs did not provide adequate information about expertise and description of the member's role in the development of the guideline, as well as the patients' preferences, so they were assigned low scores. Only the SEMICYUC-SENPE [23-32], DGEM [16], SCCM/ASPEN [2], and AND [35] guidelines described the target users. AND was a unique CPG that reached a score higher than 60% in this domain.

Domain 3: Rigor of development

The AGREE II quality scores for domain 3 ranged from 17.7% to 81.0%. Seven CPGs scored less than 60% in this domain. Procedures for updates, external reviews, and lacks in the descriptions of the systematic search methods and criteria for selecting the evidence were the most common weaknesses across all included CPGs. Only two CPGs received a score higher than 60%: ESICM [14] and AND [35].

Domain 4: Clarity of presentation

The AGREE II quality scores of domain 4 ranged from 61.1% to 94.4%. This domain was well addressed in all CPGs, with scores higher than 60% for all CPGs.

Domain 5: Applicability

The AGREE II quality scores for domain 5 ranged from 0% to 58.3%. The AND guideline received the highest score; however, it did not achieve a score of 60% [35]. Most CPGs did not explicitly mention barriers to its application and did not provide advice and/or tools to assist its application in clinical practice. In addition, the potential resource implications of applying the recommendations and monitoring criteria were not described. All CPGs received scores below 60%.

Domain 6: Editorial independence

The AGREE II quality scores for domain 6 ranged from 0% to 91.7%. This domain yielded scores above 60% for most CPGs, except for the Canadian CPG [33], SFAR [34], and BRASPEN [15] – competing interests and funding were poorly addressed in these guidelines.

Features associated with CPG quality

Table 4 shows the characteristics of the CPGs grouped by quality status. In the group of CPGs with acceptable/moderate quality, two CPGs were published in the last

five years [14,17], three had more than 14 authors [2,14,17], three were developed by a specialty society [2,14,17], three were the revised version of previously published CPGs [2,17,35], and three adopted the systematic review method [14,17,35].

Recommendations of CPGs regarding nutrition care processes

Recommendations made by the guidelines included in the current review regarding the nutrition care process of critically ill patients are presented in **Online Supplement 4**. The major recommendations for each step of the nutrition care process for critically ill patients and the relative frequency of CPGs that concurred with the recommendations are described in **Table 5**.

Nutritional screening was recommended by four CPGs [2,15,17,34], and the Nutrition Risk in the Critically ill (NUTRIC) score was endorsed by two of them [2,15]. Nutrition assessment was recommended in seven CPGs [2,15-17,23-32,34,35], and the methods for this included complete assessments [2,17,35], subjective global assessments SGA [16,23-32], and weight loss [23-32,34].

Indirect calorimetry (IC) is the gold standard for determining the energy requirement in eight of nine CPGs [2,15-17,23-35]. However, five CPGs suggest the use of predictive equations (such as the Penn-State [23-32,35] and VCO₂ methods [16,17]) or simplistic weight-based equations [2,15,16,17,33,34] in the absence of IC. The majority of the CPGs recommend a high protein diet for critically ill patients [2,15-17,23-32,34], ranging from 1.0–1.2 g/kg/d [16] to 1.5–2.0 g/kg/d [15].

Early enteral nutrition (EN) was recommended by all nine guidelines, and most recommended the enteral route as the first choice for nutrition therapy [2,14-17,33-35]. The gastric position of the enteral tube was recommended by six CPGs [2,15-17,23-32,34], preserving the post-pyloric position for patients at high risk of intolerance or aspiration. Only three CPGs made any recommendation about the formulae for administration to critically ill patients, and they endorsed the use of standard polymeric formulae [2,33,34] without fiber [16].

Five guidelines provided clear recommendations about the indications for parenteral nutrition (PN) [2,15-17,33], and all indicated that parenteral nutrition (PN) should be provided when enteral nutrition is insufficient, not tolerated, or contraindicated. The moment for PN initiation diverges between CPGs, since two of

them recommend initiating PN “as soon as possible” [2,15] and one endorses that it be started within three to seven days [17]. Only three guidelines provided information about monitoring nutrition therapy [2,15,35], and two of them did not recommend any gastric residual volume (GRV) measures as routine processes [2,15].

Recommendations made by guidelines regarding nutrition therapy for specific conditions in critically ill patients are presented in **Online Supplement 5** and summarized below:

- Diarrhea: one CPG recommends the use of early EN [14], two recommend that EN should not be automatically interrupted before the investigation of the etiology of diarrhea [2,15] and one endorses that EN should be discontinued in cases of refractory diarrhea [16].
- Renal replacement therapy: Four of nine CPGs recommend increasing protein supply [2,15,23-32,34] to 1.5 g/kg/day [15], to a maximum of 2.5 g/kg/d [2,15,23-32].
- Severe acute pancreatitis: Early EN (first 24-48 h) should be used according to four CPGs [2,14,17,23-32]. ASPEN [2] and BRASPEN [15] reported that there is no difference between the gastric and jejunal routes in this specific situation. PN should be recommended if EN is not available or if it is not tolerated [2,15,23-32]; it should be initiated one week after a pancreatitis episode [2,15].
- Sepsis: The use of immune-enhanced enteral formulae is controversial, but there was a consensus regarding the early start of nutrition therapy for this group of patients, despite five CPGs [14-16,33,35] not providing any specific recommendations for this condition.
- Hepatic failure: Dry or usual weight should be used [2,15]. Two CPGs recommend starting with a low dose of EN immediately after life-threatening metabolic derangements have been controlled [14,17]. Three CPGs recommend the use of branched-chain amino acid formulations [2,15,23-32].
- Pulmonary failure: BRASPEN does not indicate the use of formulae with ω -3 and antioxidants [15], while SEMICYUC-SENPE [23-32], Canada CPG [33], and AND [35] indicate the use of immune-enhanced enteral nutrition.

- Obesity: Only three CPGs do not provide recommendations for critically ill patients with obesity [14,33,34]. The majority of CPGs recommend the use of IC, hypocaloric diets [2,15-17,23-32,35], and high protein targets based on obesity degree, varying from 1.8 g/kg/d [16,23-32] to 2.5 g/kg/d [2,15,23-32] (using ideal body weight) or 1.3 g/kg/d (using adjusted body weight) [17].

Quality appraisal of CPG recommendations

Table 6 presents the AGREE-REX quality scores for each of the four [2,14,17,35] CPGs classified as moderate and high quality by AGREE II in the current review. None of the CPG recommendations had an overall quality score above 70%, and all CPGs scored between 30–70%, thus resulting in these being classified as moderate quality.

Domain 1: Clinical Applicability

The AGREE-REX quality scores for domain 1 ranged from 69.4% to 86.1%; the scores of three CPGs were greater than 70% for this domain [14,17,35].

Domain 2: Values and Preferences

The AGREE-REX quality scores for domain 2 ranged from 2.1% to 21.9%; no CPG recommendations received scores above 70% [2,14,17,35]. The lack of adequate descriptions of the values and preferences of target users, decision-makers, and guideline developers resulted in low scores. Patient preference items were scarcely addressed in the ESICM [14] and AND [35] recommendations.

Domain 3: Implementability

The AGREE-REX quality scores for domain 3 ranged from 37.5% to 72.2%. The AND guideline received the highest score and was the only one that achieved a score above 70% [35]. The other CPGs recommendations did not explicitly mention local applications (i.e., provide tools and resources to facilitate the implementation of the recommendations as well as mentioning barriers to its application).

DISCUSSION

Principal findings

In this systematic review, we conducted a methodological evaluation and overall assessment of nutritional care procedures of nutritional support CPGs for critically ill patients using the AGREE II and AGREE-REX tools. Nine CPGs that provided recommendations for at least one of the steps of the nutrition care process were identified. According to AGREE II, only the ESICM [14] and AND [35] guidelines achieved acceptable quality and were strongly recommended. The DGEM [16], ASPEN [2], and ESPEN [17] CPGs achieved low to moderate quality and were recommended with modifications, while the SEMICYUC-SENPE [23-32], Canadian CPG [33], SFAR [34], and BRASPEN [15] CPGs achieved low quality and were not recommended for use in clinical practice.

According to their AGREE II quality status, the ASPEN [2], ESICM [14], ESPEN [17], and AND [35] CPGs met a methodological threshold of moderate or high quality and were evaluated using the AGREE-REX tool. None of the CPG recommendations had a high overall quality according to the AGREE-REX tool; hence, the recommendations of the four CPGs cited above were classified as moderate quality.

Nutritional care procedures recommended by different societies vary greatly in terms of frequency of agreement. Guideline recommendations were consistent between most CPGs in just a few items: the use of IC to estimate energy requirements for critically ill patients, high protein administration, and the use of early enteral nutrition (24–48 hours). Additionally, the levels of evidence in most of the nutrition recommendations of all included CPGs were discrepant and based on consensus statements.

Quality of guidelines according to AGREE II

Lower quality scores were observed in the ‘applicability’, ‘stakeholder involvement’, and ‘rigor of development’ domain methodologies. According to previous CPG systematic reviews, the ‘rigor of development’ domain is considered crucial to produce evidence-based recommendations [7,9,36]. However, in the current study, seven of nine CPGs did not achieve a minimum score of 60% in this domain [2,15-17,23-34]. Similarly, four systematic reviews of CPGs observed lower scores in the methodology domains. The mean reasons for decreases in the CPGs’ scores were: they were not based on systematic reviews; there was no clear criteria used to select the evidence; there was no link between the supporting evidence and the recommendations;

there was not an external review; there was no involvement of all the required members in the guideline development group; or they lacked descriptions of the procedures for updating the guidelines [8,9,36,37]. ‘Rigor of development’ is a key component in the process of developing a CPG, and it is linked with confidence and credibility [38]. In the current systematic review, CPGs with the highest score in this domain were those that used a formal system to guide the development process and reported each step in detail [14,35]. CPGs would benefit from a more rigorous and standardized methodology and quality of evidence while preventing the use of ambiguous recommendations (i.e. ‘may be used’ or ‘uncertain recommendations’) [39].

Similar to other studies conducted for quality evaluation of the pharmacological management of chronic diseases in primary care [36], diabetes mellitus guidelines created by Chinese researchers [37], asthma guidelines [38], rehabilitation after anterior cruciate ligament reconstruction [39], and physical activity and safe movement in osteoporosis [40] CPGs, we observed that the “applicability” domain was the domain with the lowest mean score (6.3%). Making CPGs easy to implement is a crucial step toward increasing their rate of use in clinical practice [40]. Gao et al. suggested that most guideline development agencies ignored their applications, favoring the use of relevant supporting documents and as emphasizing the promotion and hindrance factors in the application process [37] instead. The potential resource implications of applying the recommendations were also poorly reported by the CPGs for critically ill patients.

The stakeholder involvement domain addresses the degree to which the guideline represents the views of its intended users [21]. The implementation of CPGs requires both the contribution and experience of the multidisciplinary medical team and the patients’ and/or family’ points of view [38]. The Canadian CPG reinforces that patients’ perspectives could not be elicited because of the inability of most critically ill patients to participate in discussions about their nutrition, due to the therapy and factors such as sedation and/or mechanical ventilation [33]. However, it is possible to access patient values and preferences via family and/or studies addressing this point of view. This aspect is crucial because the experiences of critically ill patients are linked with the quality of care in the ICU [41]. In the current systematic review, the ESICM [14] and AND [35] CPGs detailed and described this information.

Low scores in the domains cited above are a problem for the overall quality of CPGs. This was confirmed by a study that evaluated 206 Japanese CPGs published between 2011 and 2015, which showed using a regression model that domain 3 (rigor of development), domain 4 (clarity of presentation), domain 5 (applicability), and domain 6 (editorial independence) all influenced the overall assessments of CPGs. It was also revealed that item 8 (the criteria for selecting the evidence are clearly described), item 15 (the recommendations are specific and unambiguous.), item 19 (the guideline provides advice and/or tools on how the recommendations can be put into practice), and item 22 (the views of the funding body have not influenced the content of the guideline) significantly influenced the overall assessment. The same study revealed that these four items could explain 72.1% of the variance [42] observed. Therefore, these four items highlight places requiring improvements in terms of the development of CPGs.

Quality of guideline recommendations according to the AGREE-REX tool

In the current review, the CPGs included in the AGREE-REX evaluation did not meet the threshold of high quality (>70%). Lower quality scores were observed in the “values and preferences” domain, which was also observed in the few reviews that applied the AGREE-REX tool [43,44,45]. The AGREE-REX user manual reinforces the importance of considering target users, patients/population, decision-makers, and guideline developers’ values and preferences, as they influence whether the recommendations are acceptable and should be adopted in clinical practice [11]. As an alternative to access this information, Gillespie et al. highlighted CPGs that conducted an online survey of patient consumers and made stakeholders’ drafts of recommendations available as notable exceptions. The authors also point out that CPGs are more implementable when they address these aspects [43].

Although barriers exist for the inclusion of stakeholder groups in the development process, successful engagement can be obtained using approaches such as discussion and knowledge exchange between groups (e.g., multiple stakeholders in small panels), practical support (e.g., online or face-to-face meetings), and reassessment and feedback [46]. As an alternative for future CPGs, a checklist was developed to help identify specific operational strategies to meet AGREE-REX quality criteria *a priori*. It can allow the CPG development group to prioritize when there is an absence of rigorous

and feasible operational methods so that efforts can be directed to address these gaps [47].

Quality of guidelines about nutrition care processes: comparison with other publications

Specifically, in the nutrition area, a systematic review of nine CPGs for nutrition of critically ill patients published in 2016 recommended four CPGs; three were recommended with modifications, while two were not recommended [13]. We agree with this publication in recommending the AND [35] and not recommending the SFAR CPGs [13]. On the other hand, the authors recommended the ASPEN and Canadian CPGs, while we recommended the former with modifications and did not recommend the latter. In addition, we did not recommend the SEMICYUC-SENPE CPG, while the above review recommended it with modifications. These divergences can be explained by the fact that we obtained lower scores in most AGREE II domains because we strictly followed the user's manual guidance. As an example, in the 'rigor of development' domains, we observed that the ASPEN [2] CPG did not perform systematic reviews, and both the ASPEN [2] and Canadian [33] CPGs lacked a detailed evidence-based search strategy, explicit description of criteria for excluding evidence, and descriptions of the methods used to formulate the recommendations. They also did not detail how final decisions were arrived at, nor did they provide details regarding external review. In addition, the cited systematic review included two other CPGs that were not selected by us (the Australian and New Zealand Intensive Care Society CPG and University of Pennsylvania Medical Center CPG), since they were specifically designed for surgical ICUs and did not fulfill our inclusion criteria [48, 49].

A study including eight CPGs for the nutrition management of severely burned adult patients showed an overall quality score between 29.2% and 100%, and most of them also presented a score methodological rigor score that was lower than 60%. The authors identified gaps in most of the nutrition guidelines and emphasized methodological issues that could improve the quality of future guidelines concerning nutrition support among these patients [50]. Similarly, a study including 17 CPGs for the nutrition management of cancer patients showed an overall quality of CPGs that ranged from 24.4% to 94.5%, in which most of the CPGs presented scores lower than 60% in the "rigor of development" domain (range from 13.0% to 93.2%). Of the 17

CPGs included in this review, only two were strongly recommended, 11 were recommended with modifications, and four were not recommended. The authors also found that the nutritional care procedures recommended by different CPGs varied greatly [8]. Recently, a quality appraisal review of 11 guidelines for the nutritional management of patients with chronic kidney disease showed that none of them presented high quality according to the AGREE II tool, while three presented moderate quality and were recommended with modifications by the reviewers [51].

To the best of our knowledge, no systematic review of nutrition CPGs applied the AGREE-REX tool (complement to AGREE II, as recommended by the user manual) [11].

Strengths and limitations

The present review was conducted following Cochrane protocols [18] and seven large electronic databases. The strengths of this review include a registration protocol and a lack of literature search for specific languages. We appraised clinical practice guidelines using validated tools, which are the most widely used for assessing the quality of guidelines and the applicability of their recommendations. To our knowledge, this is the first systematic review of clinical nutrition practice guidelines for critically ill adult patients using the AGREE-REX tool. Four independent evaluators in both the AGREE II and AGREE-REX tools assessed all included guidelines, and the agreement between evaluators was excellent for most domains. The inter-rater reliability between reviewers was excellent in terms of the overall mean score (> 0.900) of the application of the AGREE II and AGREE-REX tools.

On the other hand, there are intrinsic limitations of some CPGs due to the absence of some information considered important in the application of the AGREE II and AGREE-REX tools. Moreover, there are intrinsic limitations related to the tools used for CPG quality assessment. The AGREE II tool does not provide a cut-off to distinguish between high- and low-quality guidelines, nor does it suggest the more relevant domains to be considered. A systematic review of 118 publications that applied AGREE II demonstrated that one-third of AGREE II users applied a cut-off to distinguish between high- and low-quality guidelines, often without clearly describing how the cut-off was generated [52]. A cut-off or a more specific description about what is more important (for example, the methodological rigors) would be useful in the

development of guideline synopses or adaptations in cases where only guidelines of a certain quality are considered. Regarding the AGREE-REX tool, even if CPGs are based on solid methods, the overall quality will be reduced when information about the values of patients, health care professionals, and funding sources is insufficiently described.

Implications for clinical practice

Guidelines are intended to promote evidence-based decisions as a way to implement them in clinical practice. It is well known that non-adherence to guidelines results in insufficient healthcare, great discrepancies in the provided care, worse disease outcomes, and increased medical costs [53-56]. However, health professionals need simple, current, reliable, and accessible guidelines while, in parallel, the demand for training health professionals in guideline usage is a priority [57-59]. These features are not fulfilled by the AND CPG [35] because it is only available for registered users that can sign in to view the topic and access it via several links on the AND website. On the other hand, the ESICM CPG [14] achieved more simplicity, which can be explained by the limited number of recommendations regarding early enteral nutrition in critically ill patients. However, it does not address all steps of the nutrition care process.

In order to improve the future development of more rigorous and high-quality CPGs, it should be noted that the aim of the current systematic review was not to criticize the existing CPGs but rather to critically appraise their development; the AGREE II tool is designed to evaluate the quality of reporting and not the clinical applicability of the guidelines. The level of complexity of CPGs and their recommendations are inversely proportional to their adoption. They should use simple, clear, and persuasive language, be properly presented and structured, and also provide summaries for an overall visualization of the main points and messages [57].

The information summarized in **Table 5** can help professionals in clinical practice to make decisions about each step of the nutritional care process for critically ill patients, as it considers all CPGs reviewed.

Implications for research

CPG developers should be familiar with guideline development standards such as the AGREE II and AGREE-REX tools, which prioritize the input of stakeholders

(including patients) and methodology presentation, thus enabling the development process to be more transparent. The present study identified gaps in the current guidelines and highlighted several methodological issues that could increase the quality of the recommendations for the provision of nutrition support among critically ill adult patients. When the research or evidence is not methodologically robust, then CPGs are considered more as “good practice statements” rather than clinical recommendations. For some questions, well-conducted randomized clinical trials are necessary to improve the quality of evidence and support recommendations that are not based only on experts’ opinions. We suggest the following questions: 1. What is the effect of different amounts of protein delivery on muscle mass and clinical outcomes in critically ill patients? 2. Is soluble fiber safe and effective for diarrhea treatment in critically ill patients? 3. Should malnourished patients receive more energy and protein than well-nourished patients in the ICU in order to improve their outcomes?

CONCLUSIONS

The methodological evaluation of the critically ill adult patient CPGs revealed significant discrepancies, especially in terms of their applicability, stakeholder involvement, and rigor of development methodologies, which exhibited poor performance and showed substantial room for improvement. Only two out of nine CPGs were identified as acceptable quality and could be recommended for daily practice. In the CPGs, the recommendations regarding the nutrition care process varied greatly and were most based on consensus statements. According to the AGREE-REX tool, the recommendations for these CPGs were classified as moderate quality. The findings of the current systematic review emphasized methodological issues that could improve the quality of future guidelines concerning nutrition support among critically ill adult patients.

Take-home message

In the last 13 years, nine CPGs for the nutrition of critically ill patients were published: only two of them can be recommended for daily practice according to the AGREE II tool, and none of the CPG recommendations have an overall quality score above 70% based on the AGREE-REX tool.

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Conflicts of interest

The authors declare that they have no conflict of interest.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

FMS, IEC and AC contributed to the conception of the study. AC, IE, PPT and FMS contributed to the acquisition, analysis and interpretation of data. AC and FMS drafted the manuscript. All authors critically revised the manuscript, provided their final approval, and agreed to be accountable for all aspects of the work ensuring its integrity and accuracy.

Consent for publication

Not applicable

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Table 1: PICAR criteria for inclusion of CPGs

Parameter	Criteria
Participants	Critically ill adult patients
Interventions	Nutrition care process
Comparator	None
Attributes	Latest version, published in the last 13 years, with explicit evidence-based development processes, with primary focus on nutrition care process in critically ill patients
Recommendation	Report at least one eligible recommendation about steps of nutrition care process

Box 1: Full PubMed electronic search strategy

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((((((((((((((((Critical Care[Title/Abstract]) OR Care, Critical[Title/Abstract]) OR Intensive Care[Title/Abstract])
OR Care, Intensive[Title/Abstract]) OR Surgical Intensive Care[Title/Abstract]) OR Care, Surgical
Intensive[Title/Abstract]) OR Intensive Care, Surgical[Title/Abstract]) OR Intensive Care Units[Title/Abstract]) OR
Care Unit, Intensive[Title/Abstract]) OR Care Units, Intensive[Title/Abstract]) OR Intensive Care
Unit[Title/Abstract]) OR Unit, Intensive Care[Title/Abstract]) OR Units, Intensive Care[Title/Abstract]) OR Critical
Illness[Title/Abstract]) OR Critical Illnesses[Title/Abstract]) OR Illness, Critical[Title/Abstract]) OR Illnesses,
Critical[Title/Abstract]) OR Critically Ill[Title/Abstract]) OR Critically Ill Patients[Title/Abstract])) AND
((((((((((((((((((((((((((((((((((((Nutrition Therapy[Title/Abstract]) OR Therapy, Nutrition[Title/Abstract]) OR
Medical Nutrition Therapy[Title/Abstract]) OR Nutrition Therapy, Medical[Title/Abstract]) OR Therapy, Medical
Nutrition[Title/Abstract]) OR Nutritional Support[Title/Abstract]) OR Support, Nutritional[Title/Abstract]) OR
Artificial Feeding[Title/Abstract]) OR Feeding, Artificial[Title/Abstract]) OR Enteral Nutrition[Title/Abstract]) OR
Nutrition, Enteral[Title/Abstract]) OR Enteral Feeding[Title/Abstract]) OR Feeding, Enteral[Title/Abstract]) OR
Force Feeding[Title/Abstract]) OR Feeding, Force[Title/Abstract]) OR Feedings, Force[Title/Abstract]) OR Force
Feedings[Title/Abstract]) OR Tube Feeding[Title/Abstract]) OR Feeding, Tube[Title/Abstract]) OR Gastric Feeding
Tubes[Title/Abstract]) OR Feeding Tube, Gastric[Title/Abstract]) OR Feeding Tubes, Gastric[Title/Abstract]) OR
Gastric Feeding Tube[Title/Abstract]) OR Tube, Gastric Feeding[Title/Abstract]) OR Tubes, Gastric
Feeding[Title/Abstract]) OR Parenteral Nutrition[Title/Abstract]) OR Nutrition, Parenteral[Title/Abstract]) OR
Parenteral Feeding[Title/Abstract]) OR Feeding, Parenteral[Title/Abstract]) OR Feedings, Parenteral[Title/Abstract])
OR Parenteral Feedings[Title/Abstract]) OR Intravenous Feeding[Title/Abstract]) OR Feeding,
Intravenous[Title/Abstract]) OR Feedings, Intravenous[Title/Abstract]) OR Intravenous Feedings[Title/Abstract]) OR
Nutrition Assessment[Title/Abstract]) 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 care
procedures[Title/Abstract]) OR Nutrition[Title/Abstract] OR Diet[Title/Abstract])))) AND (((Clinical pathway[mh]
OR Clinical protocol[mh] OR Consensus[mh] OR Consensus development conferences as topic[mh] OR Critical
pathways[mh] OR Guidelines as topic [Mesh:NoExp] OR Practice guidelines as topic[mh] OR Health planning
guidelines[mh] OR guideline[pt] OR practice guideline[pt] OR consensus development conference[pt] OR consensus
development conference, NIH[pt] OR position statement*[tiab] OR policy statement*[tiab] OR practice
parameter*[tiab] OR best practice*[tiab] OR standards[ti] OR guideline[ti] OR guidelines[ti] OR ((practice[tiab] OR
treatment*[tiab]) AND guideline*[tiab]) OR CPG[tiab] OR CPGs[tiab] OR consensus*[tiab] OR ((critical[tiab] OR
clinical[tiab] OR practice[tiab]) AND (path[tiab] OR paths[tiab] OR pathway[tiab] OR pathways[tiab] OR
protocol*[tiab])) OR recommendat*[ti] OR (care[tiab] AND (standard[tiab] OR path[tiab] OR paths[tiab] OR
pathway[tiab] OR pathways[tiab] OR map[tiab] OR maps[tiab] OR plan[tiab] OR plans[tiab])) OR (algorithm*[tiab]
AND (screening[tiab] OR examination[tiab] OR test[tiab] OR tested[tiab] OR testing[tiab] OR assessment*[tiab] OR
diagnosis[tiab] OR diagnoses[tiab] OR diagnosed[tiab] OR diagnosing[tiab])) OR (algorithm*[tiab]))

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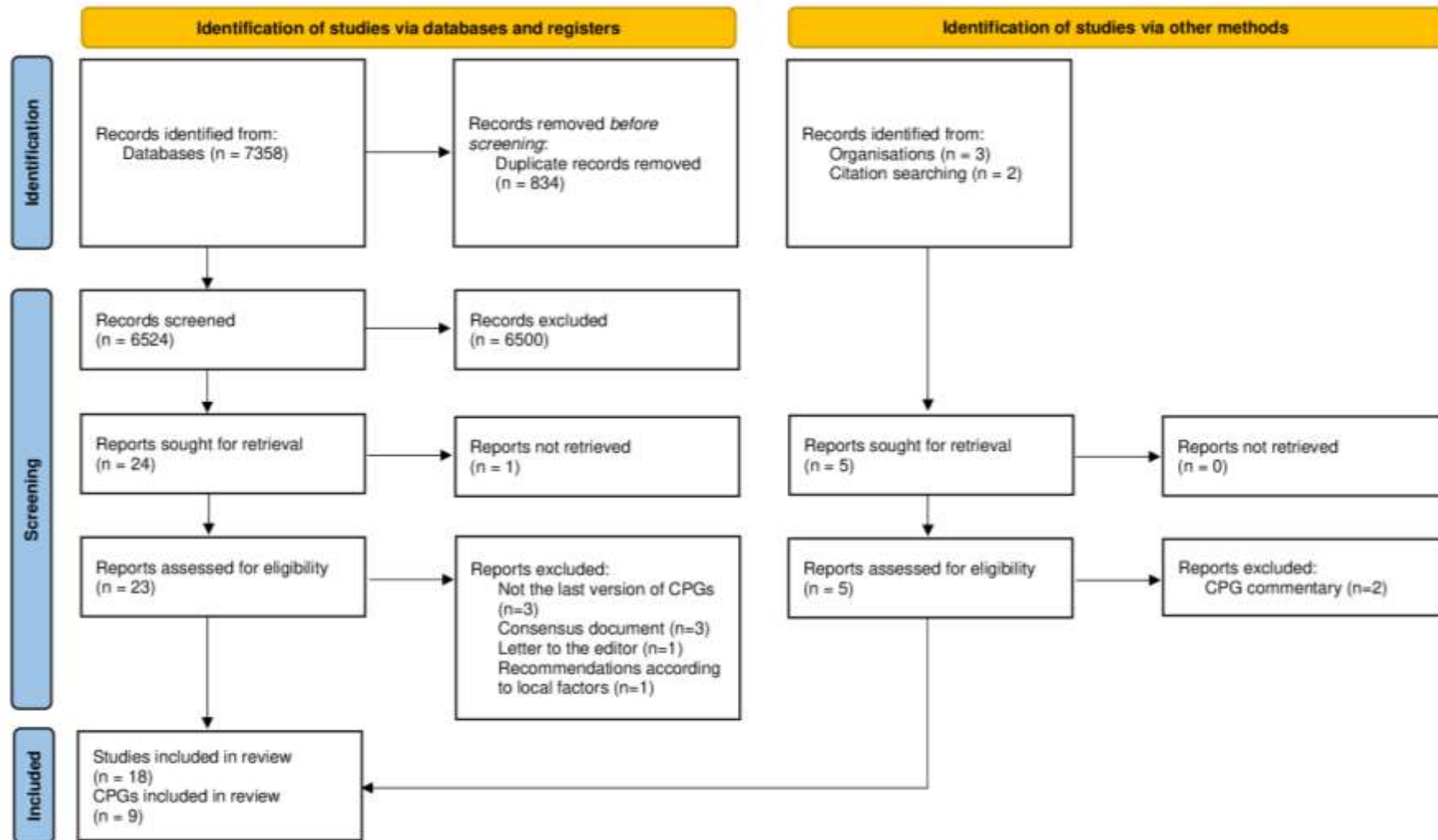


Figure 1: Study flow diagram

Table 2 - General features of eligible CPGs

Society, year [ref]	Country	Language	Update	Funding	Multidisciplinary Team	Target group	Evidence based	Grading System	Search studies period	Number of references
SEMICYUC-SENPE, 2011 [23-32]	Spain	Spanish and English	Yes	An independent external company (English translation)	21 authors Expert group	NR	Meta-analyzes and original studies	GRADE	1966 to 2010	317
Canadian, 2015 [33]	Canada	English	Yes	CIHR, CCCS, and CSCN	16 authors Epidemiologists, intensivists, surgeons, gastroenterologists, RD's, RN's and pharmacists	NR	RCTs and meta-analyses	Report only strength of the evidence	NR	NR
DGEM, 2019 [16]	England	English	Yes	DGEM	17 authors All professional groups using medical nutrition therapy	Clinicians in the interdisciplinary, intensive care unit	RCTs and meta-analyses, and observational studies	AWMF consensus statement	Up to May 2018	502
SFAR, 2014 [34]	France	French	Yes	NR	6 authors No information about team expertise	NR	NR	GRADE	NR	241
SCCM/ASPEN, 2016 [2]	United States	English	Yes	There was no input or funding from industry	14 authors Physicians, nurses, pharmacists, and dietitians	All healthcare providers involved with nutrition therapy	Meta-analyzes	GRADE	Up to December 2013	480
ESICM, 2017 [14]	United States	English	No	ESICM, IFA	24 authors	NR	Meta-analyzes	GRADE	Up to December 2015	75
ESPEN, 2019 [17]	England	English	Yes	NR	15 authors Expert group of specialists in intensive care	NR	Meta-analyzes	GRADE	Jan 2000 to Aug 2017	358
BRASPEN, 2018	Brazil	Portugues	Yes	NR	14 authors	NR	Meta-analyzes	GRADE	NR	329

[15]										
e										
and original studies										
AND, 2012 [35]	United States	English	Yes	AND	12 authors Multidisciplinary practitioners and researchers with a depth of experience in the specific field	Registered Dietitians, Advanced Practice Nurses, Health Care Providers, Nurses, Pharmacists, Physician Assistants, Physicians, Respiratory Care Practitioners, Speech-Language Pathologists, Students	Meta-analyzes	Academy's Recommendation Rating Scheme	Report the year range for each specific question	No information about number of reference

***Legend:** Academy of Nutrition and Dietetics (AND); American Society for Parenteral and Enteral Nutrition (ASPEN); Association of the Scientific Medical Societies in Germany (AWMF); Canadian Critical Care Society (CCCS); Canadian Institutes of Health Research (CIHR); Canadian Society for Clinical Nutrition (CSCN); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society of Intensive Care Medicine (ESICM); German Society for Nutritional Medicine (DGEM); Grading of Recommendations Assessment, Development and Evaluation (GRADE); International Fluid Academy (IFA); Not Reported (NR); Randomized Controlled Trials (RCT); Registered Dietitian (RD); Registered Nurses (RN); Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC); Sociedad Española de Nutrición Parenteral y Enteral (SENPE); Sociedade Brasileira de Nutrição Parenteral e Enteral (BRASPEN); Société française d'anesthésie et de réanimation (SFAR); Society of Critical Care Medicine (SCCM).

Table 3 - Standardized scores of each domain by AGREE II of CPGs

Society, year [ref]	Scope and Purpose (%)	Stakeholder Involvement (%)	Rigor of Development (%)	Clarity of Presentation (%)	Applicability (%)	Editorial Independence (%)	Mean Score Overall $\pm$ SD	Overall assessment	
								Quality	Recommendation
SEMICYUC- SENPE, 2011 [23-32]	58.3	23.6	26.0	61.1	0.0	66.7	3.0 $\pm$ 0.7	Low	Not recommended
Canadian, 2015 [33]	65.3	20.8	56.3	77.8	7.3	22.9	3.5 $\pm$ 0.83	Low	Not recommended
DGEM, 2019 [16]	61.1	41.7	34.4	77.8	7.3	66.7	3.5 $\pm$ 0.5	Low	Recommended with modifications
SFAR, 2014 [34]	13.9	25.0	31.3	66.7	6.3	0.0	2.0 $\pm$ 0.43	Low	Not recommended
SCCM/ASPEN, 2016 [2]	51.4	58.3	52.1	90.3	4.2	79.2	4.0 $\pm$ 1.09	Moderate	Recommended with modifications
ESICM, 2017 [14]	80.6	44.4	67.7	94.4	13.5	91.7	6.0 $\pm$ 0.0	Acceptable	Recommended
ESPEN, 2019 [17]	69.4	19.4	58.9	91.7	4.2	81.3	5.5 $\pm$ 0.5	Moderate	Recommended with modifications
BRASPEN, 2018 [15]	18.1	8.3	17.7	80.6	0.0	0.0	2.5 $\pm$ 0.5	Low	Not recommended
AND, 2012 [35]	83.3	79.6	81.9	81.5	58.3	72.2	6.0 $\pm$ 0.47	Acceptable	Recommended

Mean $\pm$ SD /	55.71 $\pm$ 24.69	35.68 $\pm$ 22.50	47.37 $\pm$ 21.22	80.21 $\pm$ 11.16	7.30	66.70	3.5 $\pm$ 1.4
Median (IQR)					(4.20– 10.75)	(11.45–80.25)	
ICC (95% IC)	0.845	0.837	0.912	0.798	0.288	0.935	0.925
	(0.557-0.965)	(0.535-0.963)	(0.703-0.981)	(0.428-0.953)	(-0.520-0.834)	(0.806-0.985)	(0.780-0.983)

***Legend:** Academy of Nutrition and Dietetics (AND); American Society for Parenteral and Enteral Nutrition (ASPEN); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society of Intensive Care Medicine (ESICM); German Society for Nutritional Medicine (DGEM); Intraclass correlation coefficient (ICC); Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC); Sociedad Española de Nutrición Parenteral y Enteral (SENPE); Sociedade Brasileira de Nutrição Parenteral e Enteral (BRASPEN); Société française d'anesthésie et de réanimation (SFAR); Society of Critical Care Medicine (SCCM).

Table 4. Features of Clinical Practice Guidelines grouped by quality

Feature	Acceptable and	
	Moderate Quality (n = 4)	Low Quality (n = 5)
Year of publication		
2011 – 2015	1 (25%)	3 (60%)
2016 – 2019	3 (75%)	2 (40%)
Number of authors		
≤13 (p25)	1 (25%)	1 (20%)
14-18 (median)	2 (50%)	3 (60%)
≥19 (p75)	1 (25%)	1 (20%)
Type of institution		
Specialty society	3 (75%)	5 (100%)
Governmental institution	1 (25%)	0
Region		
Developed country	4 (100%)	4 (80%)
Developing country	0	1 (20%)
Guideline version		
First version	1 (25%)	0
Updated version	3 (75%)	5 (100%)
Reported funding		
No	2 (50%)	2 (40%)
Yes	2 (50%)	3 (60%)
Method for development		
Systematic review	3 (75%)	1 (20%)
Narrative review	1 (25%)	1 (20%)
Not mentioned	0	3 (60%)

Table 5. Relative frequency of CPG that concurred with major recommendations for each step of nutritional care process for critically ill patients

Nutrition care process step	Number of CPG with specific recommendation [references]	Major recommendation	Quality of Evidence	Relative frequency of Agreement	
Nutritional screening	4	NUTRIC or NRS-2002	Moderate – Expert consensus	50%	2[2,15]/4
		All patients with high risk	Strong consensus	50%	2[17,34]/4
Nutrition Assessment	7	Complete assessment*	Expert consensus – Imperative	42.8%	3[2,17,35]/7
		SGA	GRADE C – Consensus	28.6%	2[16,23-32]/7
		Weight loss	GRADE C – Weak agreement	28.6%	2[23-32,34]/7
Nutrition Intervention - General critically ill patients					
Energy	8	IC	Weak – GRADE A	100%	8[2,15-17,23-34,35]/8
		Predictive equation (kcal/kg/day)	Expert consensus – Weak agreement	50%	4[2,15,33,34]/8
		Equations with VO2/VCO2	Uncertain – Consensus	25%	2[16,17]/8
		Penn-State	Fair – GRADE B	25%	2[23-32,35]/8
Protein	7	High protein target (> 1.2 g/kg/day)	Weak, consensus – GRADE B	71.4%	5[2,15,17,23-32,34]/7
Start	9	Early EN (24-48 hours)	Strong consensus – GRADE 2C	88.9%	8[2,14-17,33-35]/9
Route	8	EN over PN	Strong consensus – GRADE 2C	100%	8[2,14-17,33-35]/8
Position of enteral tube	8	Post-pyloric in cases of high risk of aspiration	Expert consensus – GRADE A	62,5%	5[2,15,17,23-32,33]/8
		Gastric access	Expert consensus	50%	4[2,16,17,34]/8
		Post-pyloric access	Should be considered – Fair conditional	25%	2[33,35]/8
	Enteral Formulae	4	Polymeric	Expert consensus – Weak	75%
Parenteral Indication	5	Early PN when EN is not feasible	Should be considered – Expert consensus	100%	5[2,15-17,33]/5
		Within 3-7 days	GRADE B	20%	1[17]/5
		First 7 days in low nutrition risk	Very low	20%	1[2]/5
Nutrition Monitoring	3	Not use GRV as routine	Low	66.7%	2[2,15]/3
		Measurement of GRV	Fair conditional	33.3%	1[35]/3
Nutrition Intervention - Specific condition in critically ill patients					

Diarrhea	4	Not interrupt EN	Expert consensus	50%	2[2,15]/4
		Soluble fibers	Expert consensus	50%	2[2,15]/4
Renal replacement therapy	5	High protein target (> 1.5 g/kg/day)	Weak agreement – GRADE B/C	80%	4[2,15,23-32,34]/5
	5	Early EN (24-48 hours)	Very low – GRADE A	80%	4[2,14,17,23-32]/5
Severe acute pancreatitis		Provided by either the gastric or jejunal route	Low	40%	2[2,15]/5
		PN after 1 week	Expert consensus	40%	2[2,15]/5
Sepsis	4	Early EN (24-48 hours)	Expert consensus – Strong consensus	50%	2[2,17]/4
		Specialized enteral solutions	GRADE C	25%	1[23-32]/4
Hepatic Failure	6	Not use BCAA	Expert consensus – GRADE C	50%	3[2,15,23-32]/6
		No protein restriction	Strong agreement – GRADE C	33.3%	2[23-32,34]/6
Pulmonary failure	5	Immune-modulating enteral formulas	Should be considered – GRADE B	60%	3[23-33,35]/5
	6	IC	Expert consensus – GRADE A	100%	6[2,15-17,23-32,35]/6
Obesity		Predictive equation (kcal/kg/day)	Expert consensus – GRADE B	83.3%	5[2,15,16,23-32,35]/6
		High protein target (> 1.3 g/kg/day)	Expert consensus – GRADE B	100%	6[2,15-17,23-32,35]/6

***Legend:** Academy of Nutrition and Dietetics (AND); American Society for Parenteral and Enteral Nutrition (ASPEN); Branched Chain Amino Acids (BCAA); Clinical Practice Guideline (CPG); Enteral Nutrition (EN); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society of Intensive Care Medicine (ESICM); Gastric Residual Volume (GRV); German Society for Nutritional Medicine (DGEM); Grading of Recommendations Assessment, Development and Evaluation (GRADE); Indirect Calorimetry (IC); Nutrition Risk in the Critically ill (NUTRIC); Nutritional Risk Screening (NRS-2002); Parenteral Nutrition (PN); Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC); Sociedad Española de Nutrición Parenteral y Enteral (SENPE); Sociedade Brasileira de Nutrição Parenteral e Enteral (BRASPEN); Société française d'anesthésie et de réanimation (SFAR); Society of Critical Care Medicine (SCCM); Subjective Global Assessment (SGA).

Table 6 - Standardized scores of each domain of AGREE-REX of high and moderate quality CPG

Society, year [ref]	Clinical Applicability (%)	Values and Preferences (%)	Implementability (%)	Overall assessment (%)	Quality
SCCM/ASPEN, 2016 [2]	69.4	2.1	39.6	32.9	Moderate
ESICM, 2017 [14]	86.1	21.9	58.3	51.4	Moderate
ESPEN, 2019 [17]	75.0	3.1	37.5	34.7	Moderate
AND, 2012 [35]	79.6	33.3	72.2	57.4	Moderate
ICC (95% IC)	0.748 (0.127 – 0.992)	0.959 (0.771 – 0.999)	0.858 (0.216 – 0.996)		

***Legend:** Academy of Nutrition and Dietetics (AND); American Society for Parenteral and Enteral Nutrition (ASPEN); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society of Intensive Care Medicine (ESICM); Intraclass Correlation Coefficient (ICC); Society of Critical Care Medicine (SCCM).

SUPPLEMENT MATERIAL

Online supplement 1. Full Embase electronic search strategy.

Online supplement 2. Full Cochrane Library electronic search strategy.

Online supplement 3. Individual scoring of AGREE II for each CPG.

Online supplement 4. Recommendations of CPGs and quality of evidence regarding nutrition care process steps in critically ill patients.

Online supplement 5. Recommendations of CPGs and quality of evidence regarding specific conditions in critically ill patients

Online supplement 1. Full Embase electronic search strategy.

('critical care' OR 'intensive care' OR 'surgical intensive care' OR 'intensive care unit' OR 'critical illness' OR 'critical illnesses' OR 'critically ill' OR 'critically ill patients') AND ('nutrition therapy' OR 'diet' OR 'nutrition' OR 'medical nutrition therapy' OR 'medical nutrition' OR 'nutritional support' OR 'nutrition support' OR 'artificial feeding' OR 'artificial nutrition' OR 'enteral nutrition' OR 'enteral feeding' OR 'force feeding' OR 'tube feeding' OR 'gastric tube feeding' OR 'gastric feeding tube' OR 'gastric feeding tubes' OR 'gastric feeding' OR 'intestinal feeding' OR 'parenteral nutrition' OR 'parenteral feeding' OR 'parenteral feedings' OR 'intravenous feeding' OR 'nutrition assessment' OR 'nutritional assessment' OR 'nutritional assessments' OR 'nutritional evaluation' OR 'nutrition evaluation' OR 'nutrition screening' OR 'nutrition diagnosis' OR 'nutritional screening' OR 'nutritional diagnosis' OR 'nutrition care procedures' OR 'nutrition care process') AND ('clinical pathway' OR 'clinical protocol' OR 'consensus' OR 'consensus development confereces as topic' OR 'critical pathways' OR 'guideline' OR 'guidelines as topic' OR 'practice guidelines as topic' OR 'health planning guidelines' OR 'treatment guidelines' OR guideline OR 'practice guideline' OR 'consensus development conference') AND .pt. OR 'position statement' OR 'practice parameter' OR 'best practice' OR standards OR guideline OR guidelines OR '((practice or treatment* or clinical) adj guideline*).ab.' OR '(cpg or cpgs).ti.' OR 'consensus' OR '((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol))' OR 'recommendar*.ti.kf.kw' OR '(care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti.ab,kf,kw.' OR '(algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti.ab,kf,kw.'

Online supplement 2. Full Cochrane Library electronic search strategy.

("Critical Care" OR "Intensive Care" OR "Surgical Intensive Care" OR "Intensive Care Units" OR "Intensive Care Unit" OR "Critical Illness" OR "Critical Illnesses" OR "Critically Ill" OR "Critically Ill Patients");ti,ab,kw AND ("Nutrition Therapy" OR "Medical Nutrition Therapy" OR "Nutritional Support" OR "Artificial Feeding" OR "Enteral Nutrition" OR "Enteral Feeding" OR "Force Feeding" OR "Tube Feeding" OR "Gastric Feeding Tubes" OR "Parenteral Nutrition" OR "Parenteral Feeding" OR "Intravenous Feeding" OR "Nutrition Assessment" OR "Nutritional Assessment" OR "Nutrition care procedures" OR Nutrition OR Diet):ti,ab,kw AND ("Clinical pathway" OR "Clinical protocol" OR Consensus OR "Consensus development" OR "Critical pathways" OR Guideline OR Guidelines OR Guide-line OR "Practice guidelines" OR "Clinical Practice Guidelines" OR "Health planning guidelines" OR "position statement" OR "policy statement" OR "practice parameter" OR "best practice" OR standards OR CPG OR CPGs):ti,ab,kw

Online supplement 3. Individual scoring of AGREE II for each CPG.

	Domain 1: Scope and Purpose				Domain 2: Stakeholder involvement				Domain 3: Rigour of development									Domain 4: Clarity of Presentation				Domain 5: Applicability					Domain 6: Editorial Independence		
	1	2	3	Total	4	5	6	Total	7	8	9	10	11	12	13	14	Total	15	16	17	Total	18	19	20	21	Total	22	23	Total
SEMICYUC-SENPE, 2011 [1-10]	5	6	5	16	5	1	1	7	5	5	6	4	5	7	2	4	37	6	7	6	19	1	1	2	5	9	7	5	12
Canadian, 2015 [11]	3	4	7	14	5	1	7	13	3	3	6	4	5	7	2	5	34	6	7	7	19	1	2	1	1	5	7	4	11
DGEM, 2019 [12]	6	6	6	18	5	1	7	13	7	6	7	6	6	7	1	1	41	7	7	7	21	1	1	2	6	10	7	6	13
SFAR, 2014 [13]	1	2	3	6	2	1	2	5	1	1	4	2	2	5	1	1	17	6	5	6	17	1	1	1	1	4	1	1	2
SCCM/ASPEN, 2016 [14]	6	5	7	18	4	6	7	17	6	7	7	6	6	6	6	6	50	6	6	6	18	4	5	6	1	16	7	4	11
ESICM, 2017 [15]	5	5	6	15	4	1	2	7	5	5	6	4	4	6	4	2	35	5	6	6	17	2	2	1	1	6	4	1	5
ESPEN, 2019 [16]	4	4	5	13	5	1	5	11	1	2	3	6	4	6	1	2	24	5	6	6	17	2	1	2	1	6	4	6	9
BRASPEN, 2018 [17]	2	3	2	6	4	3	2	8	1	1	5	5	4	5	1	2	24	5	4	7	16	1	1	1	1	4	1	1	2
AND, 2012 [18]	6	4	5	14	3	1	3	7	3	2	3	4	2	4	2	1	21	6	3	5	14	1	1	1	1	4	6	4	10

***Legend:** Academy of Nutrition and Dietetics (AND); American Society for Parenteral and Enteral Nutrition (ASPEN); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society of Intensive Care Medicine (ESICM); German Society for Nutritional Medicine (DGEM); Intraclass correlation coefficient (ICC); Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC); Sociedad Española de Nutrición Parenteral y Enteral (SENPE); Sociedade Brasileira de Nutrição Parenteral e Enteral (BRASPEN); Société française d'anesthésie et de réanimation (SFAR); Society of Critical Care Medicine (SCCM).

Online supplement 4. Recommendations of CPGs and quality of evidence regarding nutrition care process steps in critically ill patients.

SEMICYUC- SENPE, 2011 [1- 10]	Canadian, 2015 [11]	DGEM, 2019 [12]	SFAR, 2014 [13]	SCCM/ASPEN, 2016 [14]	ESICM, 2017 [15]	ESPEN, 2019 [16]	BRASPEN, 2018 [17]	AND, 2012 [18]
Nutrition screening								
NR	NR	NR (The authors comment that all patients have high nutritional risk)	All patients staying for >3 days in the ICU have nutritional risk. QE: Strong consensus	NRS-2002 or NUTRIC score should be performed on all patients admitted to the ICU. QE: Expert consensus	NR	All critically ill patient staying for > 48h in the ICU should be considered at risk for malnutrition QE: Strong consensus	Nutritional risk must be assessed in critically ill patients (the authors comment that NRS-2002 or NUTRIC score can be applied) QE Moderate	NR
Nutrition Assessment								
Weight loss, BMI or SGA can be used. Quality of evidence: GRADE C	NR	Criteria for disease-specific malnutrition proposed by DGEM, or SGA may be used. QE: Uncertain recommendation, consensus	BMI and weight loss. QE: weak agreement	Evaluation of comorbid conditions, function of the GI tract, and risk of aspiration. QE: Expert consensus	NR	Anamnesis, report of unintentional weight loss or decrease in physical performance, physical examination, body composition, and muscle mass and strength, if possible. QE: Strong consensus	NR (Authors recommend assessment is a good strategy to early detect and treat malnutrition). QE: Moderate	Food and Nutrition-Related History, Anthropometric Measurements, Nutrition-Focused Physical Findings, and Client History QE: Consensus, imperative
Nutrition Intervention: Energy Requirement								
1. IC QE: GRADE A 2. Penn-State University	IC or predictive equations QE: insufficient data	1. IC QE: Weak 2. Carbon dioxide (CO ₂) production	1. IC QE: Weak 2. 20–25 kcal/kg/ day, in the acute	1. IC QE: Very low 2. Predictive equations or 25–	NR	1. IC QE: B and strong consensus 2. VO ₂ from	1. IC QE: Moderate 2. 15-20 kcal/kg/day and	1. If IC is not available - Penn State University equation in non-

equation QE: GRADE B		rate (VCO ₂ method) when IC is unavailable. QE: Uncertain 3. In non-obese critically ill patients: 24 kcal/kg ABW/day QE: Weak	phase, and 25–30 kcal/kg/day after stabilization. QE: Weak agreement	30 kcal/kg/day). QE: Expert consensus		pulmonary arterial catheter or VCO ₂ derived from the ventilator will (REE = VCO ₂ x 8.19). QE: Consensus 3. 20-25 kcal/kg/day. QE: Consensus	progressing to 25-30 kcal/kg/day after the fourth day of recovering patients. QE: Low	obese, critically ill mechanically ventilated adults. QE: Fair, conditional
Nutrition Intervention: Protein Requirement								
1-1,8 g/kg/day QE: GRADE B	There are insufficient data to make a recommendation	1.0 g or 1.2 g/kg of ABW/ day QE: Weak, consensus	1.2-1.5 g/kg/day QE: Strong agreement	1.2–2.0 g/kg ABW/ day QE: Very low	NR	1.3 g/kg/day QE: 0, strong consensus	1.5-2.0 g/kg/day QE: Low	NR
Nutrition Intervention: Start of nutrition therapy								
Who are not expected to receive a complete oral diet for at least 3 consecutive days should receive nutritional support. QE: GRADE C	Early EN (24-48 hours following admission to ICU). QE: Recommended	First 24 h after ICU admission in those patients who are unable to maintain sufficient volitional intake during the early acute phase of critical illness. QE: Uncertain	EN in first 24 hours in patients who are malnourished or considered unable to eat enough within the first 3 days after ICU admission QE: Strong agreement	Early EN within 24–48 hours when patient is unable to maintain volitional intake. QE: Very Low	Early EN (in the first 48h) QE: low (GRADE 2C)	If oral intake is not possible, early EN (within 48 h) in critically ill adult patients should be initiated QE: B, strong consensus	Early EN (24-48h) in critically ill patients who cannot receive oral nutrition QE: Very Low	If EN is not contraindicated, it should be started within 24 to 48 hours following ICU admission QE: Strong, conditional
Nutrition Intervention: Route of nutrition therapy								
NR	EN over PN in patients with an intact GI tract. QE: Recommended	EN if patient is unable to maintain sufficient volitional intake QE: Weak, Strong consensus	EN over PN QE: Strong agreement	EN over PN QE: Low to Very Low	EN rather than PN QE: low (GRADE 2C)	- Oral diet shall be preferred over EN or PN patients who are able to eat. QE: GPP, strong consensus	EN instead of PN QE: Very low	EN over PN QE: Strong, conditional

						- If oral intake is not possible, EN shall be initiated rather than PN. QE: A, strong consensus		
Nutrition Intervention: Position of enteral tube								
- Post-pyloric position is not recommended QE: GRADE A - In cases of increasing GRV, high risk of aspiration or severe pancreatitis, post-pyloric position can be used. QE: GRADE C	- The routine use of small bowel feedings. QE Recommended -If routine use is not possible, small bowel feedings should be considered for patients at high risk for intolerance to EN or at high risk for regurgitation and aspiration. QE: Should be considered	Gastric access route should be preferred to the jejunal access route, except when aspiration risk/gastric residual volume is high, and when there is little technical effort to insert a feeding tube. QE: Weak, Strong consensus	Favor nasogastric or orogastric feeding tube QE: Strong agreement	- Acceptable to initiate EN in the stomach. QE: Expert consensus - Post pyloric enteral access in patients deemed to be at high risk for aspiration. QE: Moderate to high	NR	- Gastric access should be used as the standard approach. QE: GPP, strong consensus - Post pyloric in patients at high risk for aspiration. QE: GPP, strong consensus - Post pyloric in patients with gastric feeding intolerance not solved with prokinetic agents QE: B, strong consensus	-Post-pyloric position just in patients with high risk of aspiration and in those with GI intolerance. QE: moderate to high	Small bowel feeding tube placement QE: Fair, conditional
Nutrition Intervention: Type of enteral formulae								
NR	Whole protein formulas (polymeric) QE: Should be considered	Fiber-containing enteral formulas should not be used in the acute phase, when there is a high risk of intestinal ischemia.	Polymeric formulae QE: Weak agreement	Standard polymeric formula. Avoid the routine use of all specialty formulas. QE: Expert consensus	NR	NR	NR	NR

		QE: Weak, strong consensus						
Nutrition Intervention: Parenteral nutrition indication								
NR	There are insufficient data about when PN should be initiated when EN is not tolerated. QE: Insufficient data - Early PN should be considered in nutritionally high-risk patients with a relative contraindication to early EN. QE: Should be considered	If there are contraindications for an EN supply, PN should be initiated. QE: Weak, strong consensus	NR	- When EN is not feasible, exclusive PN should be started as soon as possible in patient with high nutrition risk or severely malnourished. QE: Expert consensus - In low nutrition risk patient, exclusive PN be withheld over the first 7 days following ICU admission if volitional intake can not be maintained and if early EN is not feasible. QE: Very Low	NR	- Early and progressive PN can be provided in case of contraindications for EN in severely malnourished patients. QE: 0, strong consensus - In case of contraindications to oral and EN, PN should be implemented within three to seven days QE: B, consensus	In patients with high nutritional risk in admission that cannot use GI tract, PN must be initiated as soon as possible. QE: Expert opinion	NR
Nutrition Monitoring								
NR	NR	NR	NR	- Tolerance of EN should be monitored daily and inappropriate cessation of EN and ordering NPO should be	NR	NR	Measurement of GRV must not be routinely used in critically ill patients. QE: Low	- It is recommend against holding EN when GRV <500ml in the absence of signs of intolerance QE: Fair,

				avoided. QE: Expert consensus - GRVs should not be used as part of routine care to monitor ICU patients receiving EN QE: Low				conditional - Monitor and evaluate at each visit the nutrient intake QE: Consensus, imperative
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***Legend:** Actual body weight (ABW); Academy of Nutrition and Dietetics (AND); American Society for Parenteral and Enteral Nutrition (ASPEN); Body Mass Index (BMI); Energy Expenditure (EE); Enteral Nutrition (EN); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society of Intensive Care Medicine (ESICM); Gastric Residual Volume (GRV); Gastrointestinal (GI); German Society for Nutritional Medicine (DGEM); Good Practice Points (GPP); Grading of Recommendations Assessment, Development and Evaluation (GRADE); Indirect Calorimetry (IC); Intensive Care Unit (ICU); Nil Per Os (NPO); Not Reported (NR); Nutrition Risk in the Critically ill (NUTRIC); Nutrition Therapy (NT); Nutritional Risk Screening (NRS-2002); Parenteral Nutrition (PN); Quality of evidence (QE); Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC); Sociedad Española de Nutrición Parenteral y Enteral (SENPE); Sociedade Brasileira de Nutrição Parenteral e Enteral (BRASPEN); Société française d'anesthésie et de réanimation (SFAR); Society of Critical Care Medicine (SCCM); Subjective Global Assessment (SGA).

[illegible]

Specialized NT must be initiated in the first 48 hours after resuscitation. QE: GRADE A - PN is recommended if there is some degree of intolerance or if EN is causing exacerbation of pancreatitis. QE: GRADE B - Polymeric or oligomeric formulas can be used. Post-pyloric position is indicated. QE: GRADE C	NR	NR	NR	- EN should be started at a trophic rate early. QE: Very Low - Use of EN over PN is indicated. QE: Low - EN should be provided to patient by either the gastric or jejunal route. QE: Low - PN should be considered after 1 week from the onset of the pancreatitis episode. QE: Expert consensus	Use early EN. QE: Conditional, based on low quality evidence (GRADE 2C)	Early EN should be prescribed. QE: B, strong consensus	- Use PN when not achieve 60% of the EE, after 7 days of trying EN, except in malnourished patients. QE: Expert consensus - There is no difference between gastric or jejunal of enteral tube position for GI tolerance. QE: Low	NR
Sepsis								
- PN is secure when there is no other possibility. QE: GRADE C - Enteral diets with farmaconutrients can offer benefits to septic patients' evolution. QE: GRADE C	NR	NR	Arginine-enriched enteral solution should not be administered. QE: Strong agreement	- EN within 24–48 hours, as soon as resuscitation is complete and the patient is stable. QE: Expert consensus - Not using exclusive PN or supplemental PN	NR	- Early and progressive EN should be used in septic patients after stabilization. If contraindicated, EN should be replaced by progressive PN. QE: GPP, strong	NR	NR

				with EN. QE: Very Low - Trophic feeding (10–20 kcal/h or up to 500 kcal/d) for the initial phase of sepsis, advancing after 24–48 hours to >80% of target energy. QE: Expert consensus		consensus		
Hepatic Failure								
- No contraindication for lipid emulsions, but the input should not be >1 g/kg/d. QE: GRADE C - No recommendation for protein restriction. QE: GRADE C - No recommendation for BCAA enriched diets. QE: GRADE C	NR	NR	Amino acid supply should not be decreased, except in a transient manner, in the case of encephalopathy and/or hyperammonemia. QE: Strong agreement	- Use dry weight or usual weight. QE: Expert consensus - No evidence for BCAA formulations in patients with encephalopathy who is already receiving first-line therapy with luminal-acting antibiotics and lactulose. QE: Expert consensus	Starting low dose of EN in patients with acute liver failure QE: Conditional, based on expert opinion (GRADE 2D)	Low dose EN should be administered in patients with acute liver failure QE: B, strong consensus	- Use usual weight. QE: Expert consensus - Prefer EN. PN should be an option when EN needs is not met. QE: Expert consensus - It is not recommend administration of BCAA. QE: Moderate/Low	NR
Pulmonary Failure								
EN enriched with	The use of an enteral	NR	NR	Not use high-	NR	NR	- Enteral formulas	Should be used

omega-3, gamma linolenic acid, and antioxidants may have beneficial effects. QE: GRADE B	formula with fish oils, borage oils and antioxidants should be considered. QE: Should be considered			fat/low-carbohydrate formulations to manipulate the respiratory quotient and reduce CO ₂ . QE: Very Low			with omega-3 and antioxidants are not indicated. QE: Expert consensus - Use of dense enteral formulas is indicated. QE: Expert consensus	immune-modulating enteral formulas with fish oil, borage oil and antioxidants. QE: Strong, conditional
Obesity								
- Use IC for energy requirement QE: GRADE A - For morbid obesity, hypocaloric diet (50-60% of EE, or 18-20 kcal/ kg of IBW/day) QE: GRADE B - For non-morbid obesity, hypocaloric nutrition estimated as 20-25kcal/kg of AdBW/ day. QE: GRADE C - Protein: 1,8-2,5 g/kg of IBW/ day. QE: GRADE B	NR	- Use IC for energy requirement QE: Weak, Strong consensus - 60% of the measured EE or 11-14 kcal/kg of ABW/ day if BMI 30-50 kg/m ² or 22-25 kcal/kg of IBW/day if BMI >50 kg/m ² . QE: Strong consensus -Protein: if BMI >30 kg/m ² the target of protein in the acute phase should be 1.5 g protein (or at 1.8 g amino acids)/kg of	NR	- High-protein hypocaloric feeding to preserve lean body mass, mobilize adipose stores, and minimize the metabolic complications of overfeeding. QE: Expert consensus - Enteral formula with low caloric density (1kcal/mL) and a reduced NPC:N. should be used. QE: Expert consensus	NR	- Isocaloric high protein diet, guided by IC measurements and urinary nitrogen losses should be provided. QE: 0, consensus - If IC is not available, energy requirement can be based on AdBW. QE: GPP, consensus - Protein: Guided by urinary nitrogen losses or lean body mass, and if it is not available, protein intake can be 1.3	- Low density, high protein without immunonutrients, with reduced nitrogen/non-protein calories relation formulae should be used. QE: Expert consensus - Not exceed 65%–70% of target energy requirements measured by IC. If IC is unavailable and BMI 30-50: 11–14 kcal/kg of ABW/ day or BMI >50: 22–25 kcal/kg of	- Use IC for energy requirement QE: GRADE A - For morbid obesity, hypocaloric diet (50-60% of EE, or 18-20 kcal/ kg of IBW/day) QE: GRADE B - For non-morbid obesity, hypocaloric nutrition estimated as 20-25kcal/kg of AdBW/ day. QE: GRADE C - Protein: 1,8-2,5 g/kg of IBW/ day. QE: GRADE B

		IBW/day. QE: Strong consensus		- Not exceed 65%– 70% of target energy requirements measured by IC. If IC is unavailable and BMI 30-50: 11– 14 kcal/kg of ABW/ day or BMI >50: 22–25 kcal/kg of IBW/ day QE: Expert consensus - Protein: if BMI 30- 40: 2.0 g/kg of IBW/ day or BMI > 40: 2.5 g/kg of IBW/ day QE: Expert consensus		g/kg of AdBW/day. QE: GPP, consensus	IBW/ day QE: Expert consensus - Protein: if BMI 30- 40: 2.0 g/kg of IBW/ day or BMI > 40: 2.5 g/kg of IBW/ day QE: Expert consensus	
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***Legend:** Academy of Nutrition and Dietetics (AND); Adjusted Body Weight (AdBW); American Society for Parenteral and Enteral Nutrition (ASPEN); Body Mass Index (BMI); Branched-Chain Amino Acid (BCAA); Energy Expenditure (EE); Enteral Nutrition (EN); European Society for Clinical Nutrition and Metabolism (ESPEN); European Society of Intensive Care Medicine (ESICM); Gastrointestinal (GI); German Society for Nutritional Medicine (DGEM); Good Practice Points (GPP); Grading of Recommendations Assessment, Development and Evaluation (GRADE); Ideal Body Weight (IBW); Indirect Calorimetry (IC); Not Reported (NR); Nutrition Therapy (NT); Parenteral Nutrition (PN); Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC); Sociedad Española de Nutrición Parenteral y Enteral (SENPE); Sociedade Brasileira de Nutrição Parenteral e Enteral (BRASPEN); Société française d'anesthésie et de réanimation (SFAR); Society of Critical Care Medicine (SCCM); Subjective Global Assessment (SGA).

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8 CONSIDERAÇÕES FINAIS

Tendo em vista o impacto das alterações metabólicas da doença crítica sobre a degradação do estado nutricional, e consequentemente risco nutricional e desnutrição como preditores de piores desfechos clínicos, a terapia nutricional tem papel fundamental no manejo clínico do paciente crítico. Ademais, considerando os numerosos estudos publicados sobre o tema, bem como dificuldade em sintetizar essas informações devido à sua heterogeneidade, é comum a utilização de diretrizes de prática clínica para embasar a prática clínica baseada em evidências científicas. Estas por sua vez sumarizam as etapas do cuidado nutricional do paciente crítico, e devem seguir padrões metodológicos rigorosos. Porém, as diretrizes de prática clínica, mesmo na disponibilidade de guias para seu desenvolvimento, podem sofrer influência de vieses e padrão de qualidade insatisfatória. Dessa forma, foram propostos instrumentos específicos para avaliação da qualidade das diretrizes e suas recomendações, sendo os instrumentos AGREE II e AGREE-REX os mais conhecidos e utilizados nas revisões sistemática de diretrizes clínicas disponíveis na literatura.

O presente trabalho teve como objetivo avaliar criticamente a qualidade metodológica e das recomendações de diretrizes de prática clínica para o cuidado nutricional de pacientes adultos críticos e investigar o grau de concordância entre suas recomendações. Para responder a esse objetivo, foi conduzida uma revisão sistemática de diretrizes para a prática clínica de pacientes adultos críticos utilizando as ferramentas AGREE II e AGREE-REX, a qual demonstrou discrepâncias significativas nestas diretrizes especialmente em relação à sua aplicabilidade, envolvimento das partes interessadas e rigor de desenvolvimento. De acordo com estes achados, das nove diretrizes identificadas, somente duas foram classificadas com qualidade aceitável e foram recomendadas sem modificações para uso na prática clínica de acordo com o AGREE II: a da *Academy of Nutrition and Dietetics* e da *European Society of Intensive Care Medicine*. Ademais, as recomendações das diretrizes foram em sua maioria baseadas em consenso de especialistas e tiveram variação considerável, bem como o conjunto de recomendações de quatro diretrizes avaliado com o AGREE-REX foram classificados com qualidade moderada. As principais recomendações para cada etapa do processo de cuidado nutricional para pacientes críticos foram baseadas no consenso de especialistas e para a maioria delas a frequência de concordância entre as diretrizes foi menor ou igual a 50%.

Nossos achados demonstram que a forma como as diretrizes para cuidado nutricional do paciente crítico estão apresentadas requer melhorias e que a área de nutrição no paciente crítico carece de estudos primários bem delineados para que as recomendações possam ser

estabelecidas com base em evidências científicas com maior poder para testar hipóteses.

Como implicação prática, os resultados encontrados no presente estudo podem auxiliar os profissionais de saúde que utilizam diretrizes clínicas a atentar para sua avaliação crítica. Ou seja, a partir de quesitos de metodologia e confiabilidade dos resultados das diretrizes, o profissional tem subsídio para sua tomada de decisões sobre cada etapa do processo de cuidado nutricional de pacientes críticos, decidindo criticamente por seguir as recomendações contidas nas diretrizes ou por buscar novas evidências oriundas de estudos primários de boa qualidade e/ou revisões sistemáticas com metanálise apropriadamente conduzidas.

Como implicação no âmbito da pesquisa, os resultados do presente trabalho fornecem subsídio para desenvolvimento de futuras diretrizes para cuidado nutricional do paciente crítico com descrição mais rigorosas de todo o processo de desenvolvimento, maior adesão aos guias para tal e, conseqüentemente, com maior alta qualidade. Ademais, quando os estudos primários não são metodologicamente robustos, as recomendações de diretrizes são consideradas mais como “declarações de boas práticas” do que recomendações clínicas. Dessa forma, para algumas questões referentes a diferentes etapas do cuidado nutricional do paciente crítico, ensaios clínicos randomizados bem conduzidos são necessários para melhorar a qualidade das evidências e apoiar recomendações que não são baseadas apenas em opiniões de especialistas, dentre as quais pode-se citar: a) Qual o efeito de diferentes aportes proteicos na preservação da massa muscular e nos desfechos clínicos de pacientes críticos?; b) Fibra solúvel é efetiva e segura para tratar diarreia em pacientes críticos?; c) Após estabilidade hemodinâmica, uso de fórmulas com mix de fibras podem ser benéficas para a microbiota intestinal e desfechos clínicos em pacientes críticos? ; d) Pacientes críticos desnutridos podem ser beneficiados de maior oferta calórica-proteica em comparação aos pacientes sem desnutrição?

Destaca-se ainda, que para maior aplicabilidade prática das diretrizes clínicas, faz-se necessário que a compreensibilidade e a aceitabilidade das mesmas seja independentemente avaliada previamente a sua disseminação. Ainda, os serviços de nutrição e de terapia intensiva podem discutir internamente a construção de protocolos para tomada de decisões de forma a garantir uma prática clínica baseada em evidências. Mas, previamente a isso, conforme demonstrado nesse trabalho, faz-se necessário que as diretrizes clínicas para cuidado nutricional do paciente crítico possam ser descritas com maior detalhamento para que haja a garantia de que escores aceitáveis de acordo com o AGREE-II e o AGREE-REX sejam atingidos.