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ORIGINAL RESEARCH

Guidance for assessment of the inflammation etiologic criterion for the GLIM diagnosis of malnutrition: A modified Delphi approach

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Abstract

Background: The Global Leadership Initiative on Malnutrition (GLIM) approach to malnutrition diagnosis is based on assessment of three phenotypic (weight loss, low body

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mass index, and reduced skeletal muscle mass) and two etiologic (reduced food intake/assimilation and disease burden/inflammation) criteria, with diagnosis confirmed by fulfillment of any combination of at least one phenotypic and at least one etiologic criterion. The original GLIM description provided limited guidance regarding assessment of inflammation, and this has been a factor impeding further implementation of the GLIM criteria. We now seek to provide practical guidance for assessment of inflammation.

Methods: A GLIM-constituted working group with 36 participants developed consensus-based guidance through a modified Delphi review. A multiround review and revision process served to develop seven guidance statements.

Results: The final round of review was highly favorable, with 99% overall "agree" or "strongly agree" responses. The presence of acute or chronic disease, infection, or injury that is usually associated with inflammatory activity may be used to fulfill the GLIM disease burden/inflammation criterion, without the need for laboratory confirmation. However, we recommend that recognition of underlying medical conditions commonly associated with inflammation be supported by C-reactive protein (CRP) measurements when the contribution of inflammatory components is uncertain. Interpretation of CRP requires that consideration be given to the method, reference values, and units (milligrams per deciliter or milligram per liter) for the clinical laboratory that is being used.

Conclusion: Confirmation of inflammation should be guided by clinical judgment based on underlying diagnosis or condition, clinical signs, or CRP.

KEYWORDS
assessment, C-reactive protein, inflammation, malnutrition

CLINICAL RELEVANCY STATEMENT

The original GLIM description provided limited guidance regarding the assessment of inflammation. To address this concern, a modified Delphi approach was used to develop practical consensus guidance statements in support of the GLIM etiologic criterion that includes inflammation assessment. These guidance statements should be helpful for healthcare practitioners who use GLIM and other approaches for malnutrition diagnosis. The occurrence of acute or chronic disease, infection, or injury that is often/usually associated with inflammatory activity may fulfill the GLIM disease burden/inflammation criterion. When testing is available, CRP should be measured in uncertain cases to help confirm the inflammatory character of the underlying disease or condition.

INTRODUCTION

Since the advent of the 21st century, there has been increasing awareness in the medical community of research findings that implicate inflammatory response as an etiologic factor in the development of many medical conditions and their outcomes. The development of treatments that target inflammation has changed paradigms and favorably altered the course of disease. Other diseases, although not of inflammatory origin, may also trigger inflammatory, often systemic, responses.

In the late 20th century, knowledge emerged about the role of inflammatory cytokines for catabolism in cancer and some other weight-losing conditions.[1–3] This understanding has now been extended to the recognition of inflammation as a key contributor to disease-related malnutrition.[4–15] Inflammation may promote anorexia with decreased nutrient intake, altered metabolism with increased muscle catabolism and elevated resting energy expenditure, and blunted response to nutrition interventions.[4,10] Perturbation of micronutrient levels is often observed, including reduced levels of iron, zinc, selenium, vitamin D, and vitamin A.[16–23] Severe, sustained, or recurrent inflammation promotes increased risk of malnutrition and is associated with adverse outcomes. Negative nitrogen balance may persist despite ongoing nutrition therapy.[24] Among patients with a high degree of severe inflammation—that is, C-reactive protein (CRP) > 100 mg/L—there was no beneficial effect of nutrition therapy on 30-day mortality.[25] Successful management requires treatment of the underlying disease or condition as well as nutrition intervention. Preservation and restoration of muscle mass and function are high priorities. Micronutrient deficiencies should also be addressed. Anti-inflammatory interventions, both medical and nutrition, warrant consideration. Appreciation of the contributions of inflammation therefore helps to inform the assessment of risk of developing

malnutrition, supports diagnosis of malnutrition, aids the selection of appropriate interventions, provides priority for ongoing monitoring, and guides expected outcomes.

The Global Leadership Initiative on Malnutrition (GLIM) approach to diagnosing malnutrition[13–15] includes recognition of weight loss, low body mass index (BMI), or reduced muscle mass as phenotypic criteria and the recognition of reduced food intake/assimilation or disease burden/inflammation as etiologic criteria. Fulfillment of at least one phenotypic and at least one etiologic criterion is the requirement for the diagnosis of malnutrition. Other approaches include consideration of underlying disease that may serve as a proxy for inflammation; examples include the Academy of Nutrition and Dietetics (AND) and American Society for Parenteral and Enteral Nutrition (ASPEN) Indicators to Diagnose Malnutrition (AAIM),[26] Nutritional Risk Screening (NRS)-2002,[27] Subjective Global Assessment (SGA),[28,29] and Patient-Generated SGA.[30] A recent review of GLIM studies in older adults found that a variety of approaches were being used for assessment of inflammation[31]; more than half used the diagnosis of inflammatory disease only, whereas the others mainly used CRP alone or combined with the presence of inflammatory disease.

The GLIM priority is to promote a simple global approach that will address the spectrum of healthcare settings where skilled nutrition practitioners and laboratory testing may not be readily available. The original GLIM construct description[13–15] provided limited guidance as to how to undertake assessment of inflammation in support of malnutrition diagnosis. To address this gap and to assist an array of practitioners in a wide variety of global healthcare settings, we have applied a modified Delphi approach[32] to develop guidance statements for assessment of inflammation.

METHODS

The GLIM core leadership representatives of four major global clinical nutrition societies; ASPEN, the European Society for Clinical Nutrition and Metabolism (ESPEN), the Latin American Federation for Parenteral and Enteral Nutrition (FELANPE), and the Parenteral and Enteral Nutrition Society of Asia (PENSA) appointed a working group of 10 individuals to draft the guidance statements for review. This working group included representatives of each society (Rocco Barazzoni, Renee Blaauw, Cristina Cuerda, Charlene Compher, Isabel Correia, David C. Evans, Juan Bernardo Ochoa Gautier, and Veeradej Pisprasert) and two cochairs (Tommy Cederholm and Gordon L. Jensen). Multiple virtual meetings and email communications were undertaken to review existing approaches and potential recommendations. A PubMed literature search spanning the past 25 years using inflammation and malnutrition as combined search terms revealed 597 citations (last conducted May 10, 2023). Many of these publications were disease- or setting-specific—for example, end-stage renal disease or critical care. However, a more general analysis of a merged data set of geriatric hospitalized patients from across Europe[33] found that food intake was more likely to be significantly compromised at CRP levels above 30 mg/L. Therefore, little guidance was available in the context of the more general application to malnutrition diagnosis sought by GLIM, such that extrapolation of established inflammation assessments from other specific medical conditions proved necessary.

The cochairs prepared draft guidance statements for review; a modified Delphi approach was then used to ascertain the level of agreement for each statement. An electronic survey was sent to each member of the working group that queried level of agreement on a 5-point scale as "strongly disagree, disagree, indifferent, agree, or strongly agree." Additional comments and suggestions were also requested. With each round of review, the cochairs made further edits based on the feedback received. Transparency was maintained as the feedback and revisions were promptly shared with all participants. The consensus threshold for acceptance of an individual guidance statement was set at 75% "agree" or "strongly agree."

In November 2022, the working group completed an initial review of the draft statements with comments and suggested edits without Delphi scoring. From December 2022 through February 2023, revised versions then underwent three successive rounds of review with further comments and Delphi scoring. With each round, further revision was undertaken with resulting improvements in consensus. For the last round of working group review, the levels of "agree" or "strongly agree" exceeded the required threshold for all draft statements (>90% overall).

The cochairs then constituted an extended review group of experienced physicians and dietitians with expertise in clinical nutrition to bring additional global representation and expertise to the review process. The 26 members were Ryoji Fukushima, M. Cristina Gonzalez, Andre van Gossum, Leah Gramlich, Joseph Hartono, Steven B. Heymsfield, Harriët Jager-Wittenaar, Renuka Jayatissa, Heather Keller, Ainsley Malone, William Manzanares, M. Molly McMahon, Yolanda Mendez, Kris M. Mogensen, Naoharu Mori, Maurizio Muscaritoli, Guillermo Contreras Nogales, Ibolya Nyulasi, Wendy Phillips, Matthias Pirlich, Maria D. Ballesteros-Pomar, Elisabet Rothenberg, Marian de van der Schueren, Han Ping Shi, Alison Steiber, and Marion F. Winkler. The same modified Delphi approach was undertaken by the extended review group, starting with the draft guidance statements that resulted from the working group review process. Two additional rounds of review, editing, and Delphi scoring were completed by the extended group from February through April 2023. Because additional revisions resulted from the first round of review by the extended group, the working group also participated in the second (final) round of review. Responses for the 36 total Delphi review participants are summarized in the Results section.

RESULTS

GLIM recommendations for assessment of inflammation using underlying diagnosis, laboratory indicators, and clinical signs

The final levels of agreement for each guidance statement and noteworthy comments and clarifications that constitute discussion

sections for each statement are summarized below. There were 36 total Delphi review participants, so with seven final statements, there were 36 × 7 = 252 potential responses. The overall response rate was 100%. Of the responses, 249 were "agree" or "strongly agree" (99%), three were "indifferent," and zero were "disagree" or "strongly disagree." All of the guidance statements readily met the predefined threshold for acceptance.

Statement 1: Fulfillment of the GLIM disease burden/inflammation criterion

The occurrence of acute or chronic disease, infection, or injury that is often/usually associated with inflammatory activity may fulfill the GLIM disease burden/inflammation criterion; that is, confirmation by laboratory markers is not always necessary. This is especially important when such laboratory testing is unavailable. When testing is available, we recommend that laboratory markers be measured in uncertain cases to help confirm the inflammatory character of the underlying disease or condition. The "agree" or "strongly agree" response rate to statement 1 was 100%.

Comments and clarifications on statement 1

The GLIM priority[13–15] is to promote a simple global approach that will address the spectrum of healthcare settings where skilled nutrition practitioners and CRP testing are often not available. It is therefore not possible to assume access to such practitioners or to make such laboratory testing a requirement for the guidance that we provide. In the context of the guidance statements, "acute or chronic" categories refer to the duration of the inflammatory disease or condition. The GLIM inflammation criterion does not distinguish between acute and chronic inflammation. Either will fulfill the criterion. The distinction between acute and chronic inflammation and the recognition of the severity of inflammation are helpful in discerning the risk of development and progression of malnutrition and in guiding interventions and anticipated outcomes (see statements 2 and 3). Uncertain cases would include those in which the underlying diagnosis or condition may be suggestive of inflammation, but the clinical setting or signs are inconsistent, such that measurement of CRP may help to clarify inflammatory status. Clinical judgment based on underlying diagnosis or condition, clinical signs, or laboratory markers should guide confirmation of the presence of inflammatory disease or condition (see statement 7). Because each individual must still meet a phenotypic criterion (weight loss, low BMI, or reduced muscle mass) to receive a diagnosis of malnutrition,[13–15] one cannot be diagnosed with malnutrition on the basis of meeting only an etiologic criterion. In general, the GLIM approach has had similar utility in identifying malnourished individuals and in predicting adverse outcomes as other approaches, such as SGA and AAIM.[34–45]

Statement 2: Conditions with severe or moderate acute inflammation

Confirmation of the presence of severe or moderate acute inflammation should be guided by clinical judgment based on underlying diagnosis or condition, clinical signs, or laboratory markers. The listed conditions are shared as examples that usually have severe acute inflammatory components, thus fulfilling the inflammation criterion. Such conditions include critical illness, major infection/sepsis, acute respiratory distress syndrome, severe burns, major abdominal surgery, multitrauma, severe closed head injury, and severe acute pancreatitis. Moderate inflammatory conditions can also present acutely and warrant recognition as described above. Examples would include chronic diseases complicated by acute moderate exacerbations, or acute new presentations with moderate inflammation associated with Crohn's disease, rheumatologic conditions, chronic obstructive pulmonary disease (COPD), pancreatitis, diabetes, infections, wounds, and many other examples. The "agree" or "strongly agree" response rate to statement 2 was 100%.

Comments and clarifications on statement 2

We have defined the "acute" category as rapid in onset and associated with moderate or severe inflammation. We do not include mild inflammatory conditions with the "acute" category, as a host of mild infections and other self-limited or easily treated conditions constitute these mild inflammatory states. They should receive appropriate medical treatment and be monitored. If they persist to become chronic or progress to moderate or severe inflammation, then further nutrition evaluation and intervention should be considered. A number of diseases or conditions can fit in either the acute or chronic and the mild, moderate, or severe inflammation categories depending on the duration and severity of inflammation that is manifest. Examples are pancreatitis and COPD, which are included in both statements 2 and 3.

Critically ill individuals with severe acute inflammatory conditions such as closed head injury, multitrauma injury, major abdominal surgery, or burns may not initially meet phenotypic GLIM criteria, but such individuals will readily meet the GLIM etiologic criterion for inflammatory condition. A recent prospective cohort study of intensive care patients used low adductor pollicis muscle thickness as an alternative phenotypic indicator of reduced muscle mass and found that the use of this measure with the GLIM criteria for diagnosis of malnutrition proved highly feasible and demonstrated high sensitivity, moderate specificity, and substantial agreement with SGA.[45] These patients should be assumed to be at elevated risk of developing malnutrition and warrant early nutrition intervention and follow-up. It must also be noted that a subset of intensive care patients arrives in the surgical and medical intensive care units with preexisting malnutrition. In the critical care setting, practitioners often make use of severity scores, such as Nutrition Risk in the Critically Ill (NUTRIC)[46] and Sequential Organ Failure Assessment

(SOFA),[47] that encompass inflammatory components to help guide management and expected outcomes.

Statement 3: Conditions with mild to moderate chronic inflammation

Confirmation of the presence of mild to moderate chronic inflammation should be guided by clinical judgment based on underlying diagnosis or condition, clinical signs, or laboratory markers. The conditions listed below are shared as examples that may have mild to moderate chronic inflammatory components—that is, clinical findings or laboratory markers that fulfill the disease burden/inflammation criterion. Examples of such chronic conditions include congestive heart failure, cystic fibrosis, COPD, Crohn's disease, celiac disease, rheumatoid arthritis, diabetes, abdominal obesity, metabolic syndrome, malignancies, infections (eg, tuberculosis), HIV/AIDS, pressure wounds, periodontal disease, chronic kidney disease, hepatic cirrhosis, mild/moderate pancreatitis, organ failure/transplant, and many other examples. It is important to recognize that inflammation may remit, relapse, or be exacerbated, depending on the course of disease, treatment modalities, or superimposed events or complications. The "agree" or "strongly agree" response rate to statement 3 was 100%.

Comments and clarifications on statement 3

This statement is intended not to provide a comprehensive list of chronic inflammatory conditions but rather to provide relevant examples. We deliberately encompass both mild and moderate chronic inflammatory conditions in statement 3 and do not suggest that all the highlighted examples have the same degree of inflammation. The "chronic" category is characterized by mild to moderate inflammation of at least 2–4 weeks' duration. We do not generally include severe inflammatory conditions with the "chronic" category, but there are overlapping conditions—such as "chronic critical illness" associated with Persistent Inflammation, Immunosuppression, and Catabolism Syndrome[48]—that may be reasonably assigned to the chronic category based on duration, severity of inflammation, and clinical judgment. This type of protracted, severe inflammation is often associated with a deteriorating course and poor outcomes. These patients effectively remain in the acute inflammatory state and are at extremely high risk to develop severe malnutrition and warrant ongoing nutrition intervention and monitoring.

An individual is not required to have laboratory documentation of active inflammation to meet the GLIM inflammation etiologic criterion. For example, a patient with Crohn's disease and a mild acute mucosal relapse may not have an elevated CRP level, but the patient will have a chronic condition that is associated with bouts of inflammation and will therefore satisfy the GLIM etiologic inflammation criterion. An individual does not have to have active inflammation for a disease or condition to contribute to malnutrition. First, it is common for a recent bout of inflammation that has resolved to have contributed to ongoing malnutrition. Second, as illustrated by Crohn's disease and COPD, there are a variety of chronic diseases or conditions in which inflammation may reoccur. Third, we can make a direct connection to disease-related malnutrition, as other disease-related mechanisms besides inflammation contribute to malnutrition (see statement 4). It is important to recognize all such diseases or conditions regardless of whether active inflammation is present. It must also be highlighted that GLIM determines malnutrition severity based only on the phenotypic criteria of weight loss, low BMI, or reduced muscle mass, not the etiologic criteria of disease burden/inflammation or reduced food intake or assimilation.[13–15]

Statement 4: Conditions with no clear or perceptible inflammation

Disease conditions that have no clear or perceptible inflammatory components will not fulfill the disease burden/inflammation criterion unless confirmed by laboratory analyses. Typical examples that often result in malnutrition include psychiatric diagnoses such as anorexia nervosa and depression; select malabsorptive, obstructive, or dysmotility conditions such as esophageal stricture, anatomic short bowel syndrome, and intestinal pseudo-obstruction; and neurological conditions such as dysphagia after cerebrovascular accident. To highlight the distinction, we note that there are nondisease conditions that are associated with limited resources or an environment that compromises food security, access, or intake, including poverty, famine, and war. These conditions also lack inflammatory components and often result in malnutrition. Starvation may also be complicated by recurrent infections that contribute to malnutrition. Note that malnourished individuals with conditions that have no clear or perceptible inflammatory components can be readily diagnosed with malnutrition based on the GLIM phenotypic criteria and meeting reduced food intake or assimilation as an etiology. The "agree" or "strongly agree" response rate to statement 4 was 100%.

Comments and clarifications on statement 4

Among those conditions with no clear or perceptible inflammatory components, there are select malabsorption and dysmotility conditions such as esophageal stricture, bariatric surgery complications, anatomic short bowel syndrome, and intestinal pseudo-obstruction. These conditions will generally meet the GLIM etiologic criterion of impaired nutrient intake and assimilation. They can, however, be complicated by inflammatory conditions such as aspiration, bacterial overgrowth, or hepatic dysfunction.

We are aware of reports that anorexia nervosa may be associated with altered cytokines levels and neuro-inflammation.[49,50] However, CRP level is generally not elevated and serum albumin level does not

typically decrease in patients with anorexia nervosa until there is life-threatening malnutrition or a superimposed inflammatory event.[51–53]

Statement 5: Laboratory markers indicating inflammation

The documentation of laboratory markers indicating inflammation may support confirmation of the disease burden/inflammation criterion. Use of CRP is recommended, and alternative laboratory measures are noted in the following comments and clarifications section. Due consideration of the clinical setting and known limitations of these markers must be given. The "agree" or "strongly agree" response rate to statement 5 was 100%.

Comments and clarifications on statement 5

CRP has a half-life of 19 h and therefore suffers limitations as a relatively brief point in time measure.[54] CRP is a positive acute phase reactant synthesized by the liver, so levels may be reduced in advanced liver disease. By contrast, end-stage kidney disease is associated with increased CRP levels that may be elevated because of inflammation and decreased filtration. Use of nonsteroidal anti-inflammatory drugs, magnesium supplements, or statins may lower CRP levels.[55–57] It should also be recognized that CRP and other inflammatory indicators may be reduced in patients with immunosuppressive conditions or therapies. Such patients may not meet the inflammation criterion, but they should be evaluated for the reduced food intake or assimilation etiologic criterion and associated phenotypic malnutrition criteria.

Alternative laboratory measures offer potential as inflammatory indicators, but concerns regarding sensitivity, specificity, availability, cost, and need for more extensive testing and validation apply to these measures in varying degrees. Alternative indicators of inflammation include interleukin-6, erythrocyte sedimentation rate, neutrophil/lymphocyte ratio, T-lymphocyte counts (CD3+), thrombocytosis, myeloid derived suppressor cells, serum albumin, serum albumin/CRP ratio, procalcitonin, red cell distribution width, nucleated red blood cells, hyperglycemia, hyperinsulinemia, homeostasis model assessment calculation, iron kinetics (Fe, ferritin, and transferrin), lactate, fibrinogen, and calprotectin (for inflammatory bowel disorders). Gene polymorphisms may be associated with more robust inflammatory response.[58,59] Systemic inflammatory response has also been associated with distinctive gene expression arrays.[59–61] "Omics" approaches, including genomics and metabolic phenotyping, offer promise for early recognition of individual risk for severe inflammatory response.[62–64]

There has been growing interest in the use of serum albumin level as a proxy indicator of inflammatory activity. It is a negative acute phase reactant that declines precipitously in severe inflammatory states. Long believed to be an indicator of malnutrition, strong consensus now suggests that serum albumin level lacks validity for the diagnosis of malnutrition in the setting of inflammatory conditions.[65] Inflammation promotes decreased serum albumin level by reprioritization of hepatic protein synthesis and redistribution of serum proteins through increased capillary permeability. With a half-life of 3 weeks, serum albumin level recovers slowly as inflammation abates, but it offers the advantage of being widely available as part of routine hospital admission laboratory profiles across the globe. Some practitioners combine the interpretation of serum albumin levels with CRP testing, such that if the serum albumin level is low and the CRP level is elevated, it is highly likely that inflammatory activity is manifest. Despite the well-documented limitations of using serum albumin level as an indicator of malnutrition, there remains value in measuring serum albumin level because of its utility as an indicator of inflammation and because it serves as a potent predictor of adverse patient outcomes.

Statement 6: Application of CRP testing

It is recommended that the recognition of underlying medical conditions commonly associated with inflammation be supported by CRP measurements when the contribution of inflammatory components is uncertain. For acute conditions, CRP levels ≥10 times higher than the upper reference value for the methodology of the selected clinical laboratory can be used to support the presence of moderate to severe acute inflammation. For example, CRP levels of 10–50 mg/L may be used to meet the acute criterion at a moderate level of inflammation, but CRP levels >50 mg/L support severe acute inflammation. Because critically ill patients vary in their degree of inflammation, measurement of CRP is helpful to ascertain its severity.[45] For chronic conditions, serial measures of CRP higher than the upper reference value for the methodology of the selected clinical laboratory support the presence of the chronic inflammation criterion. For example, serial measures of elevated CRP at 3.0–9.9 mg/L and 10–50 mg/L may be used to support mild and moderate inflammation, respectively. The "agree" or "strongly agree" response rate to statement 6 was 94%.

Comments and clarifications on statement 6

To interpret CRP values, consideration should be given to the methodology, reference values, and units (milligrams per deciliter or milligrams per liter) for the clinical laboratory that is being used.[66] A conversion factor of 10-fold may be used to go from milligrams per deciliter to milligrams per liter, and the accuracy of that conversion should be confirmed. Standard assays detect CRP levels of ≥10 mg/L, whereas high-sensitivity assays reliably detect CRP levels of 0.5–10 mg/L.[67] Standard low-sensitivity CRP assays are suitable for many routine clinical surveillance applications. Assessment of conditions that require detection of lower CRP levels warrants the use of high-sensitivity assays. For example, increased risk of cardiovascular disease may be detected at levels as low as 1.0–3.0 mg/L.[68] Laboratory standards and recommended thresholds for assignment of severity vary,[69] but for simplicity, we propose that

CRP levels of 3.0–9.9 mg/L are consistent with mild inflammation, levels of 10–50 mg/L are consistent with moderate inflammation, and levels of >50 mg/L are consistent with severe inflammation. These thresholds are provided to help support identification of individuals with inflammatory diseases and conditions, not to assess risk for development of disease. They are consistent with reports that moderate and severe inflammation may be associated with significant reductions in food intake in hospitalized older patients.[33]

Serial CRP measures can be helpful when the status or contribution of inflammation is unclear in the setting of a chronic condition. This approach is used routinely in the medical management of cardiovascular disease, COPD, Crohn's disease, and rheumatologic conditions. Measurement of CRP trends can be helpful, because a single normal CRP value does not exclude the possible contribution of an inflammatory component. Whenever possible, the opportunity to make use of CRP test results that have been ordered for other medical purposes is encouraged.

Statement 7: Application of clinical judgment

Clinical judgment based on the integration of underlying diagnosis or condition, clinical signs, and/or laboratory markers should guide confirmation of the presence of inflammatory disease or condition. The sound interpretation of some of these indicators requires clinical training and expertise. The presence of clinical inflammatory symptoms and signs, like fever and leukocytosis, can support the presence of inflammatory activity. Judgment is also indicated to discern when serial CRP measurements may be indicated or when alternative laboratory indicators of inflammation warrant consideration (see statement 5). Although some of these indicators may suffer limited sensitivity and specificity, they can still be used by clinicians to support the potential presence of inflammation. The “agree” or “strongly agree” response rate to statement 7 was 97%.

Comments and clarifications on statement 7

Interdisciplinary collaboration with experienced clinicians is encouraged. The development of clinical training workshops that are focused on assessment of inflammation in relation to malnutrition for practitioners with limited training or experience is warranted.

CONCLUSION

Inflammation is widely recognized as a contributor to disease-related malnutrition.[4,10] However, limited guidance as to how to undertake assessment of inflammation in support of malnutrition diagnosis and treatment has been available. In this report, we describe the use of a modified Delphi approach to develop guidance statements for the assessment of inflammation. The resulting guidance statements secured strong overall support, with 99% of the responses by the Delphi participants being either “agree” or “strongly agree.” This guidance has been developed for use with the GLIM approach to diagnose malnutrition, but it should also be helpful for healthcare practitioners who use other approaches for malnutrition diagnosis.

Key practical guidance points for the clinician may be summarized as follows. The occurrence of acute or chronic disease, infection, or injury that is often/usually associated with inflammatory activity may fulfill the GLIM disease burden/inflammation criterion. When testing is available, CRP should be measured in uncertain cases to help confirm the inflammatory character of the underlying disease or condition. Confirmation of inflammation should be guided by clinical judgment based on underlying diagnosis or condition, clinical signs, or CRP. Disease conditions that have no clear or perceptible inflammatory components will not fulfill the disease burden/inflammation criterion unless confirmed by CRP.

To promote adoption of the proposed guidance, dissemination with translation into other languages will be necessary. Priority should also be given to developing the contents for a clinical training workshop that is focused on the assessment of inflammation in relation to malnutrition and can be widely shared with practitioners with limited training or experience. We anticipate that the guidance statements will continue to evolve over time, as new research breakthroughs target priorities to develop better biomarkers of inflammation as well as better understanding of the complex interactions of inflammation and malnutrition. “Omics” approaches, including genomics and metabolic phenotyping, may ultimately facilitate individualized assessment of inflammatory risk to promote personalized treatment and care.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception of the project and to writing, reviewing, and editing. Gordon L. Jensen and Tommy Cederholm led the project from inception to completion. They contributed data curation, formal analysis, writing of the original and subsequent drafts, methodology, investigation, supervision, project administration, and validation. All authors agree to be fully accountable for ensuring the integrity and accuracy of the work, and all authors affirm that they have read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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