Disease-related malnutrition and nutritional assessment in clinical practice

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9 Summary and General Discussion

Summary of main findings

The first study **(Chapter 2)** showed that, prior to vascular surgery, a substantial proportion (24%) of patients is at medium/high risk for malnutrition. Those individuals who are currently smoking, of female gender, or being scheduled for amputation are factors associated with a risk for malnutrition in this patient population. To assess risk for malnutrition, patients completed the PG-SGA Short Form. The PG-SGA SF includes four subdomains: Weight, Food intake, Symptoms, and Activity and Function. Scores on the various subdomains of the PG-SGA SF showed that risk for malnutrition in this population was predominantly characterized by the presence of nutrition impact symptoms such as loss of appetite, fatigue, and pain combined with limitations in activities and function. This is important for clinical practice, as with this information adequate interventions can be developed to possibly improve the patients' condition prior to surgery.

To obtain evidence on the possible association between the risk for malnutrition and clinical outcome in this specific population, the frequency and severity of post-operative complications of patients after vascular surgery were evaluated **(Chapter 3).** Patients with medium or high risk for malnutrition (PG-SGA SF score of four points or higher) were more likely to experience a higher number and/or more severe post-operative complications. This implies that healthcare professionals need to be aware that these patients may be in need of interdisciplinary interventions to reduce the risk of complications after surgery.

To determine the level of knowledge on malnutrition and nutrition-related disorders, a survey among 369 dietitians in Belgium, Norway, Sweden, and the Netherlands was performed **(Chapter 4).** Respondents were asked to give a definition of malnutrition and to provide a diagnosis on three cases regarding starvation, cachexia, and sarcopenia. Definitions provided by the respondents were compared to the conceptual definition of malnutrition of the European Society for Clinical Nutrition and Metabolism (ESPEN). Forty-one percent of the respondents scored sufficiently on the question about the definition. Thirty-one percent of the respondents provided a correct diagnosis on three cases of nutrition-related disorders. In addition to this, the percentage of dietitians with sufficient knowledge regarding both the concept of malnutrition and providing correct diagnoses was low (13%). As few dietitians know the differences between the nutrition-related disorders, as a consequence, patients may not receive adequate treatment.

To gain an insight in how malnutrition is assessed and treated in patients with tuberculosis, a review of literature was performed **(Chapter 5)**. It was identified that a nutritional assessment instrument that covers all three domains of the conceptual definition of malnutrition was used in only two (6%) of the studies included in the review (n=35). Six of the 17 nutritional intervention studies that were included in the review did not perform nutritional assessment at baseline. Primary outcome measures of most of the nutritional intervention studies were generally those other than nutritional parameters such as resolution of chest radiograph abnormalities or rifampin exposure, and only 53% of the studies

reported results with regard to a nutritional parameter. For clinical practice these results imply that only the most severe cases of malnutrition are being identified and the less severe cases may be untreated.

Ultrasound measurement is a relatively new method for the assessment of muscle mass. The exploratory study on the added value of ultrasound measurements in patients with COPD **(Chapter 6)** relates ultrasound measured muscle size with fat-free mass index measured by bioelectrical impedance analysis, and function as assessed by handgrip strength and five times sit to stand test. The results showed that the size of the rectus femoris is moderately strong related to fat-free mass index and muscle strength in patients with COPD. In the future, ultrasound measured muscle mass may play an important role in the assesment of peripheral muscle in clinical practice.

In the study described in **(Chapter 7)** the coexistence and relationships between malnutrition, frailty, physical frailty, and disability were explored in patients with COPD. In these patients, malnutrition and frailty substantially coexist (40%). Although the prevalence of each of the four conditions is quite high, the coexistence of all four conditions is limited (11%). This research was important as with this knowledge of the complexity of the relations between the different conditions, adequate interdisciplinary interventions may be identified to improve the health status of these patients.

The qualitative study on dietary resilience in patients with COPD **(Chapter 8)** showed that patients with severe COPD experience food-related challenges with regard to grocery shopping, cooking, and eating. The key themes of motivation for dietary resilience in these participants were: 'Wanting to be as healthy as possible', 'Staying independent', and 'Promoting a sense of continuity and duty'. Despite their motivation and the strategies they developed to deal with their individual food-related challenges, the majority of patients with severe COPD did not meet the criteria for a healthy diet. For healthcare professionals it is important to take notice of the strategies and the key themes of motivation to eat healthy in patients with severe COPD, as these may be helpful to other patients.

Interpretation of the main findings and clinical implications

In 2003, the Academy of Nutrition and Dietetics adopted the 'nutrition care process' (NCP) to provide dietitians with a framework for critical thinking and decision-making.[1] The NCP is a systematic approach to providing high quality nutrition care and consists of four distinct, interrelated steps: assessment, diagnosis, intervention, and monitoring.[1] Clearly, if patients are not initially screened for malnutrition, they will not be identified as being at risk. Consequently, patients will not be assessed and diagnosed as malnourished nor treated appropriately.[2] Guidelines regarding clinical nutrition have described strategies for adequate nutritional screening, assessment, counselling, therapy, and monitoring.[3-6] Nevertheless, malnutrition is still rarely prevented and is often unrecognized and thus left untreated despite its preventable and generally treatable nature.[2,7] Reasons for this lack of prevention and

recognition appear to be a lack of time, money, awareness, and knowledge.[8-12] Therefore, developments in areas that inhibit progression are required.

Education

The topic of malnutrition needs to become more profoundly embedded in the curriculum of the educational programs on, for example, Nutrition and Dietetics, to improve the level of knowledge and skills on the prevention and treatment of malnutrition in future generation dietitians. In addition, nutrition education for healthcare professionals such as physicians and nursing staff is needed to improve awareness and knowledge on the topic of malnutrition so that they can enhance awareness among their patients as well. Furthermore, post-educational training is needed to improve knowledge and skills regarding malnutrition in dietitians that already work in clinical practice so that they can intensify nutritional knowledge in other professionals and their patients.

The enhancement of awareness was addressed by the study that 'profiled' patients prior to vascular surgery, which can be beneficial in selecting groups of patients for screening purposes. This study showed that the use of a comprehensive instrument such as the Patient-Generated Subjective Global Assessment (PG-SGA SF) identifies nutrition-related problems that characterize risk for malnutrition thus enabling triaging for interventions. The PG-SGA SF identified that, in this population, risk for malnutrition was characterized by the presence of nutrition impact symptoms combined with limitations in activities and function. No difference was determined in the body mass index (BMI) between the low risk and medium or high risk groups, and a majority (54%) had a BMI of ≥25 kg/m^2, indicating being overweight or obese. This finding shows that, although BMI is often used as a criterion for the assessment of malnutrition, it has no discriminating power in clinical populations. In general and in clinical practice as well, malnutrition is still considered as a construct that is connected to being underweight, e.g., the cachectic phenotype. In our society, this majority of patients have a normal or even high BMI.[13] However, patients at a height of 1.78 m and a weight of 95 kg have a BMI of 30 kg/m^2. After a 20% weight loss, their BMI is still 'normal' with 24 kg/m^2, and the patient is likely to be malnourished and may experience severe implications of malnutrition in daily life.

In the study on malnutrition and frailty in patients with COPD, malnutrition was primarily characterized by loss of appetite, fatigue, feeling full quickly, and experiencing a dry mouth. For example, in a highly catabolic disease, patients may score more points in the domain of weight loss than those prior to having vascular surgery. This may be explained by the double burden of disease-related malnutrition. Adequate nutritional intake is threatened by loss of appetite and, simultaneously, the caloric intake is not used efficiently. In addition, inflammation activity related to the underlying disease or its treatment causes breakdown of muscle protein.[3] This is why it is crucial to use an instrument to assess and monitor malnutrition that addresses both anabolic factors (food intake and activity) and catabolic factors

(e.g., fever and use of corticosteroids). The PG-SGA comprises items related to the intake of food as well as nutritional requirements and, therefore, gives comprehensive insight into the (lack of) balance between nutritional intake and requirements.

In addition to the recommendation to use a comprehensive instrument such as the PG-SGA (SF), it is also important to create awareness that nutritional screening is probably most beneficial when the earliest signs of risk for malnutrition occur. This should preferably occur at the beginning of the pathway aimed at diagnosis and/or treatment of the disease in the clinical outpatient setting or in primary care. Standard screening procedures for assessment and monitoring of malnutrition, therefore, should be implemented in the primary care and outpatient settings as well and not just in hospitals. In the Netherlands, screening for malnutrition at admission is implemented in hospitals which has increased awareness among healthcare professionals and policy makers.[14] However, most patients experience only a brief time in the hospital, and the time to fully treat malnutrition during that hospital stay is too short. Treatment and monitoring of malnutrition, therefore, should be transferred to the outpatient setting or primary care.

If dietitians do not have the nutritional knowledge to screen and assess (risk for) malnutrition or a nutrition(-related) disorder/condition, this may lead to over- or under-diagnosing of malnutrition and subsequent inadequate treatment of patients. Screening for and assessment of malnutrition requires a sufficient level of knowledge of the concept of malnutrition. If the fundamentals, i.e., the different domains (imbalance of nutritional intake, body composition, and functionality), of the definition of malnutrition are insufficiently known or understood, this will pave the way for inadequate assessment methods that do not address all of the domains of the concept.[15,16] In the survey among dietitians, a low percentage (13%) of dietitians with 'sufficient knowledge' regarding malnutrition, starvation, cachexia, and sarcopenia was ascertained.

Starvation (i.e., 'hunger-related malnutrition') implies a pure deficit of the intake of food leading to gradual loss of fat as well as muscle tissue.[3,17] Thus, starvation is not related to a physical disease and is not accompanied by inflammation activity. Cachexia is a subtype of disease-related malnutrition that has been defined as "a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass".[17,18] Cachexia, therefore, is characterized by severe catabolism. Whereas cachexia is related to a chronic or subacute disease, sarcopenia is characterized by age-associated loss of muscle and function.[19] Clinical signs of malnutrition or a nutrition(-related) disorder/condition may overlap as each involves muscle wasting to a certain extent, however, the underlying mechanisms profoundly differ. Therefore, differentiation has therapeutic and prognostic implications.[3] In contrast to starvation, optimal nutritional therapy may not completely reverse the breakdown of muscle mass in cachectic patients, although this is related to the advancement of the cachectic process. In addition, anti-inflammatory therapy

and exercise may be indicated for optimal treatment.[20] Furthermore, sarcopenia is multifactorial; not only protein deficits play a role, but also hormonal changes and immobility.[21]

Insufficient nutritional knowledge is likely to result in inadequate nutritional care in clinical practice.[22] In addition, without sufficient knowledge, dietitians cannot empower patients to cope with nutrition-related impediments and will not be able educate other healthcare professionals regarding this topic.[23] A lack of knowledge may also be an explanation for the outcome of the scoping review: only 6% of the methods used to assess malnutrition in patients with tuberculosis actually align with the entire construct of malnutrition. This finding implies that the prevalence of malnutrition in patients with tuberculosis is currently unknown and that some patients may not receive the nutritional intervention that they need.

The enhancement of nutritional knowledge in healthcare should not be limited to dietitians. Interventions for malnutrition are often interdisciplinary, for example, nausea can be treated with nutritional counselling and intervention and simultaneously with anti-emetic drugs. Limitations in activities and function may be addressed by combined advice from a dietitian and a physiotherapist in which the dietitian may discuss a schedule for adequate protein intake that accords with the patient's habits and daily activities and aligns with the training schedule from the physiotherapist. Another field of interdisciplinary collaboration is pharmacy. Many different drugs are prescribed in a dose that is based on the effectiveness of the drug in a person of a certain body weight. However, the changes in body composition due to malnutrition or any other nutrition(-related) disorder/condition may influence the exposure to drugs and therewith the risk of toxicity, as suggested by studies in patients with cancer.[24] Therefore, it is important that other healthcare professionals learn about the basic nutritional concepts such as nutritional screening, nutrition-related disorders/conditions, and their treatment. Shared knowledge could enhance collaboration to the benefit of the patient. For example, if the professional who performs general pre-operative screening in the weeks before surgery notices that the patient is at risk for malnutrition or is malnourished, then there is still time to intervene before the surgery and improve the patient's outcome. Thus, next to enhancing the level of nutritional knowledge in dietitians, nutritional education should be embedded in educational programs of physicians and other healthcare professionals.[25,26] Physiotherapists and nurses are involved in the pre- and rehabilitation of many of the patients that are malnourished. They need to be aware of how malnutrition inhibits the patient's recovery and how they can contribute to the prevention and treatment of malnutrition.

Practical considerations

The lack of time that is reported to be one of the obstacles inhibiting progression of nutritional screening and assessment in any healthcare setting can be addressed by implementing a feasible time-saving instrument. The PG-SGA (SF) is an instrument that can improve

work flow in clinical practice due to its patient-generated nature.[27] For example, as the patient can complete the form in the waiting room before the appointment with the healthcare professional, the PG-SGA (SF) can save the professional time. Moreover, using the PG-SGA (SF) may improve the quality of interaction between the healthcare professional and the patient by having the items of the PG-SGA (SF) serve as a topic list during these interactions.[27] The PG-SGA SF provides a score, and its simple questions provide guidance to the required interdisciplinary interventions depending on the components that generate the scores. This means that the healthcare professional can easily identify which problems must be focused on in order to improve nutritional status.

There is a need to use an instrument that can identify most of the nutritional risk factors across the spectrum of diseases. The PG-SGA is an instrument that does this. For example, due to the nature of the disease and treatment, some patients may experience taste changes while others may experience nausea, fatigue, or limitations in activity. Factors underlying nutritional risk were identified in the studies performed in patients prior to vascular surgery and in those with COPD. Patients of different populations were thus identified with partly overlapping and simultaneous different nutrition related impediments who were in need of different interventions. These interventions may be interdisciplinary and vary, for example, from providing a personalized diet that corresponds with the patient's preferences in taste, more frequent smaller meals containing specific amounts of nutrients, a mealtime schedule adjusted to the patient's daily routine, prescription of pain reducing drugs, and/or specific training/exercise.

Malnutrition is not a disease-specific construct, therefore, even though many different instruments are currently being employed for different patient populations, there is no need. For elderly patients, the Mini Nutritional Assessment (MNA) has been validated and, therefore, is often used.[28] For patients with cancer, the Scored Patient-Generated Subjective Global Assessment (PG-SGA) is considered the reference method.[29] The Malnutrition Universal Screening Tool (MUST), Short Nutritional Assessment Questionnaire (SNAQ), and Nutrition Risk Screening 2002 (NRS 2002) are also among the widely used screening instruments.[30-32] An explanation for this tendency to utilize different instruments for different patient populations may be that, although malnutrition is not disease-specific, the factors underlying malnutrition may vary widely. However, these factors are only represented in the instruments to a limited extent.

Uniformity of screening and assessment of malnutrition is important since different nutritional screening and assessment instruments identify different patients as being at risk for malnutrition.[33-35] The use of different instruments, therefore, is likely to lead to disturbances in the continuum of the nutrition care process, for example, in the event of a transfer to another hospital or care facility. In the first hospital, the patient may be screened and assessed as malnourished and provided with nutritional care accordingly whereas, in the next hospital, another screening instrument could be utilized that does not identify the

patient as being at risk. This may cause inadequate care and is confusing the patient. Thus, consensus on the use of screening and assessment is urgently needed.

Methodological considerations

The first international consensus diagnostic criteria for malnutrition have been published during the course of this thesis project in 2015:

> *"Alternative 1: BMI < 18.5 kg/m²*
>
> *Alternative 2: Weight loss (unintentional) > 10% indefinite of time, or >5% over the last 3 months combined with either BMI <20 kg/m² if <70 years of age, or <22kg/m² if ≥ 70 years of age or FFMI <15 and 17 kg/m² in women and men, respectively"* [36]

These ESPEN criteria have provided clear and generally applicable criteria for the assessment of malnutrition that are independent from etiologic mechanisms. However, these criteria are subject to scientific discussion for their validity ever since their publication in part because they do not reflect the domain of food intake and function that derive from the conceptual definition and partly because BMI is of limited relevance in clinical populations. [37-39] A low BMI is a hallmark of chronic malnutrition that includes the loss of both muscle and fat tissue. However, in clinical practice, using predominantly BMI is of limited relevance for the assessment of malnutrition since, in disease-related malnutrition, mainly muscle tissue is lost, and even a minimal loss of muscle tissue has significantly negative consequences with regard to functioning.[37]

The ESPEN criteria have been validated against the PG-SGA as a reference method.[40] A study in hospitalized patients demonstrated that the ESPEN criteria have a low sensitivity and a very high specificity. These results imply that the ESPEN criteria identify only those patients that are severely malnourished and underestimate the prevalence of malnutrition since the mildly to moderately malnourished patients are not identified.

The conceptual definition of malnutrition states that insufficient intake or uptake of nutrients leads to decreased fat-free mass, diminished physical and mental function, and impaired clinical outcome.[17] The core of the definition is the insufficient intake of food. This leads to a decrease of fat-free mass, diminished function, and impaired clinical outcome. However, it seems plausible that the impaired clinical outcome cannot be part of the construct as it is a future consequence, therefore, it cannot be measured in the present. It is debatable whether measurability should be a factor of importance when defining a construct. With regard to the construct of risk for malnutrition: this in itself is a condition that predisposes for impaired clinical outcome.[17] The word 'risk' implies that there is the potential of becoming malnourished but, in fact, there can already be a decline in nutritional status but to a limited extent. It could be argued to add 'pre-malnutrition' to the

current terminology to specify this group of patients. The risk for malnutrition may then be used for patients with risk factors who do not yet have any decline in nutritional status.

For the assessment of nutritional risk and nutritional status in the studies included in this thesis, the PG-SGA or the PG-SGA SF was used. The PG-SGA (SF) was selected because the aim was to use an instrument that covers all of the domains of the definition of malnutrition.[15] In addition, the PG-SGA has been very well established as a reference method for malnutrition.[27] It has been validated in cancer and non-cancer populations but not in all patient populations.[41-44] However, since malnutrition is not a disease-specific condition, construct validation does not appear to be a necessary next step. However, studying the predictive validity of the PG-SGA in additional patient populations is recommended. Malnutrition by definition negatively impacts functionality and clinical outcome, however, the extent to which it does may differ widely per population. This difference is hypothesized to be caused by the underlying disease and its hallmarks, e.g., highly catabolic, curable, treatment, comorbidities, and nutritional guidance.

When the PG-SGA is studied in a 'new' population, it would be useful to perform an in-depth analysis of which patients within a certain population are specifically at risk. This can be beneficial if there is not enough time to screen everyone. Healthcare professionals are then informed which subgroup may be specifically at risk. However, the hallmarks of this risk for malnutrition may differ per population.

Healthcare professionals sometimes experience their first acquaintance with the PG-SGA professional component, in particular the physical examination, as comprehensible but difficult.[45] Evidently, the reliability of the PG-SGA depends on its adequate use by means of a thoroughly executed cross-cultural translation if the English language is not the standard and trained dietitians/ healthcare workers. Other researchers have shown that a course aimed at increasing knowledge significantly improves perceived barriers in working with the PG-SGA.[46,47] Training may also ensure reliability of the measurements.[48]

The studies in different patient groups that are reported in this thesis had a cross-sectional study design. Therefore, no causal relationships and only associations could be determined. The reported associations nevertheless generated hypotheses for future research. For the study on the coexistence of malnutrition and frailty in patients with COPD, the data were prospectively aggregated and cross-sectionally analyzed as a first step. There is a need for prospective data analyses with a sufficient follow up time to determine how coexistence changes over time during rehabilitation.

Future research

The next step would be to perform randomized controlled trials aimed at studying the effect of interdisciplinary interventions in patients to prevent or treat malnutrition and therewith improve clinical outcomes. The effects of oral supplements have been studied, and evidence for benefits on nutritional and clinical outcome parameters is limited. The presence of

cachexia in patients with COPD may cause the limited efficacy of simple oral nutritional interventions that do not address the metabolic disturbances associated with cachexia.[49] In order to adequately intervene upon malnutrition there is a need to perform an assessment of its specific subtypes. Malnutrition is an umbrella term, and several different subtypes exist including acute or chronic disease-related malnutrition with inflammation, for example, cachexia.[17] Since the aetiology of these subtypes differs, nutritional therapy may differ as well as the prognosis of the success of the nutritional intervention.

In addition, studies should focus on the effect of treatment on possible reversibility of frailty status. The dynamics of the relationship between malnutrition and frailty need to be assessed in longitudinal studies in different populations. Since only the relationship between malnutrition and physical frailty is thus far being studied, frailty and malnutrition together seem to be understudied. Such studies appear to be urgent since the prevalence of frailty is so high in chronic disease populations such as those with COPD. Malnutrition may be a risk factor for frailty but may also be a consequence of frailty. Learning more about this relationship may help to focus on specific interventions. A recent review on the prevention or reduction of frailty in community-dwelling older adults reported on several successful intervention strategies. Exercise was reported as being a successful moderator of frailty also in combination with a nutrition intervention or in combination with a nutrition and cognition intervention.[50] However, the studies included in this review were aimed at reducing physical frailty and not multidimensional frailty in community dwelling older adults and not in patients with a chronic disease.[50] Nevertheless, as frailty is a dynamic multidimensional system, it is plausible to suspect complex interactions between the various contributing factors that may need simultaneous intervention.

From the research performed for this thesis emerges that patients with a chronic disease who are not assessed as being at risk for malnutrition or being malnourished may nevertheless experience difficulties with their diet. These are patients that do not lose weight or muscle but do experience nutrition impact symptoms that may raise barriers for healthy food intake. Therefore, patients with a chronic disease, even if not malnourished, may still have an inadequate diet. From the Dutch National Consumption Survey 2007-2010 it can be learned that the majority of the Dutch population does not meet the lower limit of recommended vegetable and fruit consumption: percentages vary between 1% up to 14% and 3 up to 26%, respectively, depending on the age gender group. Furthermore, most Dutch adults do not meet requirements for bread and dairy products.[51] In a study on barriers for eating healthfully in a general population, the primary challenges were reported to be "financial resources, daily habits, fondness of 'good' [meaning tasteful] food, time constraint and lack of will power".[52] Hardly any of these were mentioned by the patients in the study on dietary resilience, indicating that eating healthy is difficult for many people; the nutrition-related challenges in patients with COPD are indeed disease-specific. The non-achievement of a healthy diet by patients with a chronic disease may be addressed from this

perspective. Achieving and maintaining a healthy diet is a basic need for anyone, including patients with a chronic disease. Healthcare professionals must address this need by showing an interest in their patients' diets. Future research should aim at identifying additional areas that impact the achievement of a healthy diet in patients with chronic disease.

Concluding remarks

This thesis showed that a substantial part of the patients is malnourished or at risk for malnutrition, whereas these patients may be unrecognized and thus not treated. Therefore screening and assessment are important, and should be performed in such a way that all domains of malnutrition are represented, as well as the underlying factors that give guidance to interventions. Insight in what motivates people to eat healthy and new methods to measure body composition can be helpful to the nutrition care process. This is important as (risk for) malnutrition is a predictor of worse clinical outcome and is associated with frailty. To improve recognition of malnutrition and nutrition-related disorders, more knowledge and awareness is needed. Such a change may empower both the patient and healthcare professionals to improve the patient's nutritional status and functioning.[23]

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