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AIDS Rev. 2021;23:153-161

Nutritional assessment in the HIV-infected older population receiving antiretroviral therapy

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Abstract

Malnutrition is a pronounced public health issue which often seems underestimated in the older people living with HIV (PLWH) virus infection. PLWH are highly vulnerable to nutritional problems resulting from aging-related deterioration, disease itself, and adverse effects of antiretroviral therapy (ART). The comprehensive nutritional assessments are necessary to perform routinely in this population to monitor and provide appropriate interventions to reduce comorbid conditions. In this review, we focus on the untoward impacts of malnutrition and nutritional assessments on the morbidity and mortality in the older PLWH. Some predictive factors of nutritional status in this group of patients are discussed. We propose the important components for nutrition assessment tool for older PLWH on ART. Highlighted issue is the need for developing uniform standardized tools for the early diagnosis of malnutrition in this population. Applications of the nutritional assessments, proper nutritional interventions, and regular monitoring of nutritional status in older PLWH living in every clinical setting may help the patients get better well-being. (AIDS Rev. 2021;20:153-161)

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Keywords

Malnutrition. HIV. Aging. Antiretroviral therapy. Complication.

Introduction

Malnutrition is a critical health problem in older people. In HIV infected patients, poor functional status and disease progression can be highly predicted by malnutrition[1]. HIV infection has been known to contribute to serious public health concerns. Global statistics showed that about 38 million people are living with HIV in which about 25.4 million patients are receiving antiretroviral therapy (ART)[2]. ART is widely used to suppress HIV viral loads to improve disease symptoms, health status, and treatment outcomes in people living with HIV (PLWH). According to the modeling study by Smit et al.[3], the proportion of older PLWH population (aged 50 years or above) is estimated to increase up to 73% of overall PLWH by 2030. However, beside the increase in life expectancy as the benefit of ART, a considerable number of older patients face complications resulting from both HIV and treatment regimens. Some common clinical features include bone demineralization, dyslipidemia, food intake problems, and multiple chronic comorbidities which can adversely affect the nutritional status of the older population[4,5]. In addition, loss of muscle mass or lipodystrophy represents as one of the most common complications among the older PLWH[6]. In general, geriatric population has high susceptibility to nutritional problems than

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Received in original form: 31-05-2021
Accepted in final form: 04-11-2021
DOI: 10.24875/AIDSRev.21000051

younger people. Regardless of effective viral control, HIV-infected people with good immunological function are still more vulnerable to complications than general population. In fact, malnutrition is one of the geriatric complications, which represents usually in combination with micronutrient deficiencies, and frailty which is a reduction in physical capacity[7,8]. Screening for malnutrition through monitoring weight loss and appetite loss are also included in "Integrated Care for Older Persons" and frailty screening process[8]. Therefore, the complex relationship of the older PLWH and nutritional problems becomes the important topic that we need to focus on.

Causes of malnutrition are varied from inadequate intake, impaired absorption, impaired digestion, increased nutrient requirement in specific circumstances, and excess nutrient losses[9]. Lower CD4 counts, co-infections such as tuberculosis, and long-term ART could predict poor nutritional status in some PLWH[10,11]. In PLWH receiving ART, complications such as abnormalities in metabolic panels, and negative effects on bone or muscle due to side effects of ART lead to dysregulation of physiological functions and impaired absorption of nutrients[12]. Some of the characteristics of malnutrition contain weight loss, muscle wasting, vitamin deficiencies, and susceptibility to secondary infections. HIV infection has a complicated negative relationship with malnutrition which gives rise to immune dysfunction and metabolic syndromes such as hypertriglyceridemia, increased plasma free fatty acid and hormonal abnormalities[13,14]. The negative impacts of HIV on nutritional status include common symptoms such as wasting and opportunistic infections which provoke progression of viral replication[4]. It has also been reported the negative effects of some micronutrient deficiencies on nutritional status followed by HIV progression[15]. In HIV-infected patients, severe malnutrition is a lethal occurrence which may be associated with poor medication adherence, and failure of response to ART[4,16]. Malnutrition leads to decreased immune functions and worsening of clinical outcomes in PLWH. In turn, immunocompromised PLWH have increased energy requirement which leads to malnutrition[16]. Therefore, nutritional optimization is very pivotal in the HIV population, especially in the older PLWH.

The purpose of this review is to discuss the nutritional assessment methods and significance of nutritional status in HIV-infected older population which generally is a less commonly discussed group. Studies which focused on the nutritional status of the older population are still required to carry out with a wide application of assessment methods. The rising complications due to malnutrition in older PLWH are more likely to be aggravated than general aging population. This narrative review is conducted by searching on ScienceDirect, Google Scholar, PubMed, Web of Science, and Scopus. The primary targeted study population is older PLWH whose nutritional status was assessed by various methods. Any regimen of the ART is included. Because of the limited literatures, we have compiled research articles that investigated the nutritional status in the targeted group regardless of their research primary outcomes. Full-text articles which are accessible in English language were reviewed.

Screening and assessment of nutritional status

To identify and monitor nutritional problems in older patients, nutrition care process should be recognized and applied regularly. Nutritional screening and assessment are the first step of nutrition care process aiming to identify the individuals who are malnourished or at risk of malnutrition[9,17]. Nutrition screening tools are simple to promptly identify nutritional problems before applying specific assessment methods. Based on the results of screening, further assessment methods are typically chosen. The methods should be easily applicable, validated, and acceptable to both patients and health care providers as well as evidence-based decision supports. The most extensively used screening and assessment tools in the older population are subjective global assessment (SGA)[18,19], mini nutritional assessment (MNA)[20] either in its full or short form, malnutritional universal screening tool (MUST)[21], simplified nutritional appetite questionnaire (SNAQ/SNAQ65+)[22,23], geriatric nutritional risk index (GNRI)[24], and nutrition screening initiative (NSI)[25]. Many of which could help monitoring patients with food insecurity in addition to their ability to predict nutritional issues in general and HIV-infected population. SGA values could be able to predict mortality risk and could help clinicians notice subtle changes of patients[18]. MNA is a worldwide validated tool for the assessment of nutritional status in older population including PLWH[26,27]. It has been applied in several countries using regional languages with high specificity and sensitivity. Likewise, the MUST also has been validated in many clinical settings including community care, outpatient, and inpatient clinics. Moreover, one of the strengths of the tool is that it can be applied without information about height or weight of patients[21]. The SNAQ has been widely used in nursing home and community older

people to predict appetite and weight loss. It has been used in the HIV-infected Brazilian people showing that the nutritional risk was higher in patients with food insecurity. However, the risk was less common in patients with higher quality of life[28]. SNAQ65+ has a good estimate of mortality among older people in clinical and community settings[22,23]. Another predictor of mortality and morbidity in older population is GNRI which can identify the nutrition-related health problems[24]. Therefore, the tool can help nutritional support team to monitor patients with at risk of malnutrition or malnourished. Among the older patients with poor nutrient intake, NSI can help predicting nutritional issues in clinical practice[25].

These screening tools have long been used in the aging studies, including community or hospitalized people and HIV-infected population as well. The combined methods were suggested so that the nutritional status can be predicted specifically for better results and more precise conclusions[29]. The specific information usually evaluated by these tools in various older populations are demonstrated in table 1.

Nutritional assessment with anthropometric, biochemical, clinical and/or dietary evaluations can classify patients into normal condition, at risk of malnutrition and malnourished. Each nutritional assessment method has its own benefits and drawbacks which two or more methods are usually applied in clinical studies.

Anthropometric assessment

Anthropometric measurement is one of the most conventionally used methods which can estimate body fat, muscle, and bone mass. It includes physical examinations such as weight and height for body mass index (BMI) calculation, measurements of body circumferences (at mid-upper arm, waist, hip, calf, etc.), and skinfold thickness. In HIV population, weight loss is associated with untoward clinical outcomes. To identify HIV-associated wasting syndrome, serial weight measurement has been recommended. Furthermore, BMI could be able to predict the progression of HIV infection into AIDS[30]. The application of simplified anthropometric assessments was supported by Phantom Z-score for skinfold which has been used to differentiate lipodystrophy in PLWH[31]. Anthropometry also contains more sophisticated methods such as bioelectrical impedance analysis (BIA), dual-energy X-ray absorptiometry (DEXA), magnetic resonance imaging (MRI), and computed tomography (CT). BIA mainly measures the electrical volume through the body composition, in particular total body water (TBW) and fat free mass (FFM). In contrast, the body fat is the main nonconductive tissue being resistance to the electrical current. With this principle, BIA is a noninvasive method to estimate TBW, extracellular water, intracellular water, FFM by multiple frequencies[32]. Low phase angle z-score of BIA was found to have correlation with nutritional parameters such as weight loss, BMI, body circumference and albumin in HIV-infected individuals[33]. On the other hand, higher phase angle was a good predictor of the longer survival of HIV-infected patients receiving ART[34]. DEXA has better precision which can be used to estimate bone mineral density in addition to fat mass. The bone mass and soft tissue can be distinguished using low or high energy source in DEXA[35]. DEXA was the most common method reported in the body composition measurement among the HIV population[36]. The whole body or regional body composition can also be highly predicted by MRI which has been considered quite accurate assessment. In certain clinical scenario, CT scan at the third lumbar spine (L_3) is used in both quantitative and qualitative determination of skeletal muscle mass primarily in colorectal cancer patients[37]. However, validations of those methods to measure body compositions in HIV-infected older population receiving ART are currently limited. There is still an argument on the appropriateness of the methods to evaluate the changes in body compositions of the older PLWH on ART. Since the aging process may lead to reduced bone mineral density and lean tissue mass, the comprehensive anthropometric measurements may be developed specifically for this group of patients. ART-related adipose tissue alterations have also been presented as lipodystrophy or abdominal fat accumulation[38,39]. Any anthropometric tests should be performed as a part of clinical follow-up plan in the older PLWH on ART. In addition to unintentional weight loss, mid-upper arm circumference and waist to hip ratio may be an additional promising parameter with reasonable burden in practice[40,41].

Biochemical assessment

Biochemical parameters contain either routine laboratory tests or specific nutritional-related indicators according to signs and symptoms of the patients. Serum laboratory indices such as albumin, hemoglobin, glucose and lipid profiles can determine nutrient concentrations, disease severity, organ functions and risks of related diseases. Low albumin concentration was significantly correlated with high mortality rate in

Table 1. Tools for malnutrition diagnosis in older population[18,20,21,23,24,25]

Components	Tools						Our proposed components in the specific tool for older PLWH on ART
	SGA	MNA	MUST	SNAQ65+	GNRI	NSI	
Anthropometry	Weight loss	– BMI – Weight loss – MAC – CC	– BMI – Weight loss – MUAC	Weight loss	– Current weight – Usual/ Ideal body weight	– Current weight – Ideal body weight	– Weight change compared to usual weight – BMI – MUAC – WHR
Biochemical measurements	None	None	None	None	Albumin	None	(If any) Albumin Lipid profiles
Clinical assessment	– GI symptoms – Functional impairment – Physical examination – Stress–related disease	– Functional impairment – Neuropsychological problem – Physical examination	– Physical examination – Stress–related disease	Appetite loss	None	– Disease – Oral problem – Food affordability	– Any signs of lipodystrophy at face, limb, and abdomen – Functional tests
Dietary history or intake	Yes	Yes	Yes	Yes	None	Yes	Yes
Scores							
Normal	A	24-30	0	Weight loss < 4 kg, MUAC ≥ 25 cm	> 98	≤ 2	Gap of validation
At risk of malnutrition or malnutrition	B	17-23	1	-	92-≤ 98 (low risk) 82-< 92 (moderate risk)	3-5	
Severe malnutrition	C	< 17	≥ 2	Weight loss ≥ 4 kg, MUAC < 25 cm	< 82	≥ 6	

SGA: subjective global assessment; MNA: mini nutritional assessment; MUST: malnutrition universal screening tool; SNAQ: simplified nutritional appetite questionnaire; GNRI: geriatric nutritional risk index; NSI: nutrition screening initiative; BMI: body mass index; MAC: mid-arm circumference; CC: calf circumference; MUAC: mid upper arm circumference; WHR: waist-hip ratio; GI: gastrointestinal.

older patients[42]. Low serum albumin concentration (< 3.5 g/dL) was also associated with disease progression, AIDS mortality, and all-cause mortality in HIV patients[43,44]. Hemoglobin, glucose, and total cholesterol are also useful biomarkers of malnutrition in older adults[45]. Insulin resistance and dyslipidemia is generally found in older PLWH receiving ART. Abnormality of the lipid profiles may be caused by the pathophysiology of the HIV infection in addition to ART regimens[38]. The effects of ART on metabolic parameters were recently reviewed elsewhere[39].

Clinical assessment

Clinical assessment comprises examination of physical function, medical histories, appetite, and possible comorbidities. The presence of opportunistic infections, fever, and diarrhea should be aware and assessed regularly. Clinical features can express nutrient deficiencies; for example, muscle or bone tenderness may indicate vitamin D deficiency, or explicit the side effects of the treatment. Inspection of lipoatrophy and lipohypertrophy at face, limb and abdomen is included in the safety monitoring parameters after starting ART. Functional tests are also necessary to perform in older patients to indicate the muscle function and physical activity. Several methods have been validated in HIV-infected adults on effective ART including Fried's Frailty Phenotype, The Short Physical Performance Battery (SPPB), and the 400-m walk[46]. Handgrip strength, 5-time chair stand test, 6-m walk, or SPPB can be co-evaluated with body composition analysis (either DEXA or BIA) to diagnose aging sarcopenia in clinical settings[47,48]. Validations of those parameters in the HIV-infected older population receiving ART are still warranted.

Dietary assessment

Nutritional assessment tools involve with dietary assessment as an important component. Representation of the diet intake can be done either retrospectively or prospectively including food diary, food frequency questionnaire, and nutrient intake analysis[17]. These methods assess types, amounts and quality of food consumption, fluid and alcohol intake, history of food allergies, route of administrations, and diet accessibility. Due to an old individual's memory limitation, short-term 24-h recall, or semiquantitative food frequency questionnaire may be favorable. It was reported that the widely used methods for dietary assessment in HIV population were 24-h recall and food frequency questionnaires[36]. Direct observation before and after meals during hospitalization is a good option to reduce portion estimation error but it is almost impossible to do in community-based dwellings. Caregivers or family members should contribute to long-term care by providing proper food supply and taking part in monitoring diet intake of older PLWH[49]. Nutritional education program for patients and caregivers is one of the effective ways to improve nutritional status, ART adherence, and treatment outcomes[50].

It cannot be assumed that one definite method is better than another, and there is no method of choice or no gold standard method for the assessment of nutritional status in HIV-infected patients yet. The choice of assessment methods should depend on the target population and the aim of the study[36]. Applications of combined nutritional assessments may be helpful in the timely identification of malnourished people so that effective nutritional supports may be provided before serious adverse events occur. Some assessments applied by the previous studies in older PLWH are briefly described in supplementary table 1.

Vulnerability of the older PLWH and predictors of nutritional status

In general, HIV attacks helper-T cells and causes a significant reduction of CD4 count which leads to dysregulation of immune functions and production of inflammatory cytokines such as interleukins (IL-4, IL-10), interferon gamma and tumor necrosis factor alpha[51]. The process of viral replication also becomes hasty, and there is a significant drop of immunity due to reduced CD4/CD8 cells. Susceptibility to opportunistic infections, significant loss of body weight, lean body mass, vitamins and minerals, and increased food and nutrient requirements are the major impact factors on the nutrition status of PLWH. Due to malnutrition, lymphoid tissue mass, lymphocytes and phagocytic function become decreased. The overall result is a decrease in body defense system followed by an increase in co-infection rate[52]. Therefore, immune deficiency and malnutrition are interrelated to each other in HIV infection. Following the increased risk of coinfections, nutrients and energy are depleted especially when the patient's CD4 count is < 200 cells/mm^3. In the previous study in Ethiopia, malnutrition was more prominent in adult PLWH with CD4 counts < 200 cell/mm^3 [53]. It was noted that low CD4 counts were indicators of abnormal nutritional status even in most younger PLWH[10,11].

Thus, it is important to consider the relationship between CD4 counts and malnutrition in older PLWH who are vulnerable to nutritional abnormalities. In fact, nutritional problems themselves usually lead to impaired immunological status of the older people regardless of HIV infection. Compared to uninfected population, older PLWH had higher risk of malnutrition[27]. Basically, in HIV-infected population, physiological function becomes impaired with the advance in age. It was reported that HIV progression or death was independently predicted by older age (50 years or above) in addition to association of baseline CD4 count and progression to AIDS[54]. The older PLWH are highly susceptible to advanced infections due to immune impairment[51]. The most prominent outcome is wasting which has been known as a significant predictor of morbidity and mortality[55]. Some comorbidities which lead to malnutrition include gastrointestinal problems, parasite infections, tuberculosis, and pulmonary insufficiency, thereby increasing risks of anorexia, anemia, cachexia and sarcopenia[56]. Moreover, the iatrogenic risk such as renal toxicity in HIV-infected older patients has been increased due to malnutrition[7].

The role of BMI is very important regarding the nutritional status of HIV population. BMI was used as an indicator of nutritional status in the older PLWH aged above 60 years[29]. Low BMI was associated with abnormal nutritional status in PLWH aged 50 years and above[27]. Likewise, it was found to be the most important risk factor of bone demineralization[57]. Body weight and BMI of older PLWH were considerably lower than uninfected people[57]. Moreover, lower BMI was found as a strong predictor of mortality in HIV population receiving ART[40]. A previous Ethiopian study of PLWH on ART showed that malnutrition (BMI < 18.5 kg/m^2) was associated with increased risk of AIDS defining illness (HR = 2.27, 95% Confidence interval: 1.416, 3.625, p = 0.001)[58]. Malnutrition shares the similar physiological patterns with sarcopenia in older population because nutritional problems and weakness of muscle are usually accompanied with the increase in age[48]. The prevalence of sarcopenia can be assessed by body composition measurements using DEXA, and muscle strength measurement. Sarcopenia was found to be associated with older age, vertebral fractures, and lower BMD in the older PLWH aged 50 years and above[59]. The functional status of the body also normally declines with the increase in age. In an aging HIV population study by Erlandson et al.[60], the decrease in physical function was associated with factors such as low lean body mass (odds ratio [OR] 1.1 [1.0-1.2]) and low bone mineral density at hip (OR 3.8 [1.1-12.5]) and lumbar spine (OR 2.3 [1.1-4.5]). Of note, poor physical activity was explored as one of the determinants of bone mineral density in a case-control study of older HIV-infected and uninfected men[5]. Despite high vitamin D concentrations, HIV-infected older men had low BMD at hip, radius, and tibia than uninfected men. Physical activity and frailty were associated to each other in a cohort of the older PLWH[61]. Moreover, poor physical performance and weakness were the primary markers of frailty in this population which were represented by 49.4% and 19.9%, respectively. In a study by Bernaud et al.[7], there were 25.5% malnourished, 21.6% at risk of frailty and 2.9% frail in the older PLWH aged over 75 years.

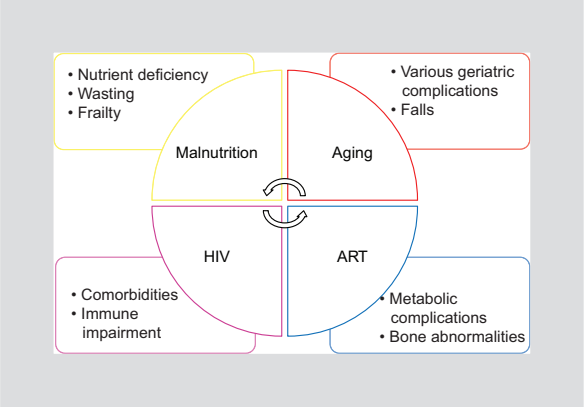

Figure 1. *The cycle of abnormal nutritional status and HIV infection in the older population receiving ART.*

There were some studies which explored the prevalence of abnormal nutritional status in older PLWH. Foreman et al.[26] explored the nutritional condition of PLWH aged above 50 years using the MNA for the assessment of nutritional status. Five percent were malnourished and 28 % were at risk of malnutrition. In addition, the assessment of bone quality in this study showed that poor nutritional status was associated with low cortical bone quality. There were about 18% of malnourished Asian older PLWH aged above 50 years in the study by Apornpong et al.[27]. They applied BIA for body composition measurement and biochemical parameters such as albumin and metabolic profiles in addition to MNA for the assessment of nutritional status. The study showed that low-fat mass was independently associated with abnormal nutritional status. Another important factor, dietary pattern can determine food quality in the older population. In the older PLWH, food insecurity was represented by 55% and that was

independently associated with poor dietary intake[62]. Accessibility of food should be promoted by giving dietary or clinical interventions in aging PLWH under low socioeconomical condition as well. The description of the interrelation among HIV infection, ART, aging and the nutritional problems are described to the point (Fig. 1).

Recommendation and conclusion

In younger PLWH, some kinds of nutritional interventions such as lipid-based supplements improved body weight, lean body mass, and grip strength with an increase in immune recovery[63]. Previously, it was observed that micronutrient supplementation might decrease the mortality rate of younger PLWH with CD4 < 200 cells/mm^3 [64]. However, nutritional supplementation as a crucial management option in malnourished older PLWH has not been stated explicitly yet. Understanding the barriers and facilitators associated with nutritional status can help implementing strategies for intervention and management in the older PLWH. For instance, it is required to understand the immunological factors which would be predictive of immune deficiency and poor nutrition in vulnerable older PLWH. In a study of PLWH with opportunistic infection like tuberculosis, malnutrition was found as a significant predictor[58]. In addition, patients receiving stavudine- or zidovudine-based regimen were more likely to develop opportunistic infections than tenofovir-based regimen[58]. Further investigations among older PLWH regarding nutritional problems and superinfections are still required. Besides, lipodystrophy and other HIV-induced wasting syndrome should be diagnosed early so that metabolic comorbid conditions leading to nutritional problems could be resolved promptly. Prospective studies about the nutritional status of older PLWH which adopt combined assessment methods are required. Since physiological changes and high vulnerability in older PLWH, there is a gap for developing uniform standardized tools for the early diagnosis of malnutrition in this population. For optimal nutritional assessment, the above-mentioned parameters are necessary to combine to determine nutritional status effectively and correctly. Moreover, older PLWH with geriatric complications or at risk of nutritional problems are recommended to get nutritional interventions timely so as not to be deficient in bone density or to reduce fracture risk and other comorbid problems[26]. In addition, the quality of life of the older PLWH could be successfully improved by implementing these strategies. Individuals with higher quality of life would have lower nutritional problems. The previous study of PLWH explored the significant association of nutritional risk and food insecurity and quality of life[28]. Nonetheless, there is still a need to examine the causality of these associations, social determinants of health and nutritional assessments are required to carry out in the older PLWH. The impact or consequences of these nutritional interventions on physical function and body compositions such as muscle, bone fat or nutritional markers should be studied longitudinally. In addition, longitudinal assessments of nutritional status in the vulnerable older PLWH may be able to monitor follow-up changes. Another fact is that household food insecurity was significantly associated with malnutrition in PLWH from resource limited areas[10,11]. Nutritional status of older PLWH in low- and middle-income countries are still necessary to monitor since the past data are limited. Therefore, addressing nutritional problems in these settings should be implemented by various assessments and interventions.

Since the life expectancy of PLWH becomes increased, clinicians in various health care settings need to be aware of age-related complications and subsequent disease progression in older PLWH. Regarding the nutritional status specifically in the HIV-infected aging population, the studies are very limited, and the scopes of the previous literatures are not wide enough yet. Furthermore, the optimal predictive factors are scattered because the focus of the studies are based on different aspects. Therefore, because of the limited evidence about this topic, numerous further researches focusing primarily on the nutritional status in the older PLWH by applying comprehensive nutritional assessments are highly recommended.

Supplementary data

Supplementary data are available at DOI: 10.24875/AIDSRev.21000051. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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