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Trabajo Original

Otros

Nutritional status and quality of life in HIV-infected patients

El estado nutricional y la calidad de vida en pacientes infectados por el VIH

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Abstract

Introduction: Nutritional status and the progression of the human immunodeficiency virus (HIV) are interlinked; though some studies have looked at the impact nutritional status has on quality of life (QoL) in patients with chronic diseases, few have studied this in HIV-infected individuals.

Objective: To investigate the relationship between nutritional status and QoL in adults with a recent HIV diagnosis.

Methods: Individuals with an HIV diagnosis performed in the fourteen months prior to a medical visit to one of Lisbon's central hospitals were eligible. Nutritional status was assessed by anthropometry, body composition analysis, and dietary intake. QoL was assessed using the WHOQOL-HIV-BREF questionnaire. Sociodemographic and clinical data were also considered.

Results: Fifty-one subjects were eligible for enrolment; the majority were male, Caucasian, employed, single, and under highly active antiretroviral therapy (HAART). Lower QoL scores were observed in subjects with inadequate energy intakes, reported weight loss, and a high waist circumference in bivariate analysis ($p < 0.05$); the same variables influenced QoL negatively after adjusting for confounders in multivariate analysis ($p < 0.05$). Various sociodemographic characteristics such as level of education, age, gender, and current health problems also predicted QoL significantly ($p < 0.05$).

Conclusion: Various aspects of nutritional status were responsible for the variations observed in QoL, suggesting a potential for nutritional intervention in improving QoL in this population.

Key words:

HIV. Nutritional status. Quality of life.

Resumen

Introducción: el estado nutricional y la evolución del virus de inmunodeficiencia humana (VIH) están interconectados. A pesar de que algunos estudios hayan visto el impacto del estado nutricional en la calidad de vida (CdV) en pacientes con enfermedades crónicas, pocos han estudiado sus efectos en pacientes infectados de VIH.

Objetivo: investigar la relación entre el estado nutricional y la CdV en adultos recientemente diagnosticados de VIH.

Métodos: cumplieron los criterios de inclusión los individuos diagnosticados de VIH en los 14 meses previos a una visita al hospital central de Lisboa. El estado nutricional fue evaluado por antropometría, análisis de la composición del cuerpo, y dieta, mientras que la CdV fue evaluada usando el cuestionario WHOQOL-HIV-BREF. También fueron considerados los datos sociodemográficos y clínicos.

Resultados: fueron seleccionados 51 individuos, la mayoría de sexo masculino, caucásicos, empleados, solteros y en tratamiento antirretroviral de gran actividad (TARGA). Varias características sociodemográficas, como el nivel de educación, la edad, el sexo y el estado de salud actual, fueron importantes indicadores del nivel de CdV ($p < 0,05$). Se observaron niveles de CdV más bajos en individuos con dietas inadecuadas, pérdida de peso comprobada y elevado perímetro de cintura en análisis bivariado ($p < 0,05$). Las mismas variantes influenciaron negativamente la CdV tras haber ajustado los factores de confusión en análisis multivariado ($p < 0,05$).

Conclusión: varios aspectos del estado nutricional influyeron en las variaciones observadas en la CdV, lo que sugiere que una intervención a nivel nutricional podría mejorar potencialmente la calidad de vida en esta población.

Palabras clave:

VIH. Estado nutricional. Calidad de vida.

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INTRODUCTION

Nutrition has always played a role in human immunodeficiency virus (HIV) care, but changes in the disease pattern, a fall in mortality rates, and hence a longer life expectancy, have led to changes in the goals nutritional support in this population (1). This has drove attention to quality of life (QoL) as an important health care indicator, given the chronicity of the disease (2). QoL is influenced by "physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment", according to the World Health Organization (WHO) (3). A better QoL has been observed in healthy populations compared to patients with chronic diseases (4,5). The relationship between nutrition, QoL and immune dysfunction, such as that seen in HIV, is interconnected (1); the disease progression is associated with a decline in nutritional status and immune function, even during highly active antiretroviral therapy (HAART) (6). However, a decline in nutritional status alone can also weaken the immune system and hence, increase the risk of infection and mortality (1,7). Malnutrition and HIV therefore have a negative effect on each other by acting synergistically on the immune system, and consequently affecting QoL (7). It is important to understand the impact nutritional status has on these patients' physical and mental health (3), since they are known to predict QoL. In the general population, lower anthropometric measurements are not only associated with a lower QoL, but being overweight or obese and having a high waist circumference have also been associated to morbidity and an impaired QoL (8).

Like with any other chronic disease, the risk for malnutrition in HIV is high (9) and, therefore, it is fundamental to assess the nutritional status of this population at regular intervals. Although it is well established that an improved nutritional status results in a better QoL in certain chronic diseases (10), this relationship is still unclear in HIV. Studies on this topic are scarce especially in the western world (1,11-13). Outside Europe, some have suggested a good nutritional status to improve QoL in HIV-infected individuals (1). Lower anthropometric measurements have been correlated with a lower QoL (11).

Nutritional status could have a positive impact on QoL by assisting in symptom management (11), improving HAART absorption and tolerance, and delaying the progression of HIV (14). The impact nutritional status has on QoL in HIV patients needs to be further explored to potentially tailor nutritional support to achieve gains in QoL.

The aim of this study was to investigate the impact nutritional status has on QoL in a sample of HIV-infected adult patients. Sociodemographic and HIV clinical-related variables were also considered.

MATERIALS AND METHODS

SUBJECTS

The sample included outpatients followed at one of Lisbon's central hospitals (for their HIV appointment). Those previously identified from clinical records as having a recent HIV diagnosis were eligible for enrolment. On the day of the visit, they were asked if they were willing to participate in the study; they were given a brief explanation describing the purpose of the study and what it involved, and the right to refuse to participate. Eligible subjects included: a) patients who had tested positive for HIV in the 14 months prior to the start of the study; b) those who were followed at the hospital for the first time in 2015 or 2016; and c) subjects who agreed to participate in the study. Data was collected between the 4th of January and the 1st of April 2016. Exclusion criteria included: a) subjects under eighteen years of age; b) pregnant women; c) subjects who did not respond to the WHOQOL-HIV-BREF questionnaire; and d) those who did not speak Portuguese or English.

SOCIODEMOGRAPHIC AND CLINICAL DATA

Sociodemographic data collected included gender, age, race, level of education, employment status, and marital/relationship status. Regarding clinical data, date of diagnosis, year of infection, mode of transmission, HAART regimen (yes/no), HIV single tablet regimen (yes/no), past opportunistic infections, current medication, medical history, current problems, current drug use (yes/no), and physical activity (yes/no) were recorded. Subjects under HAART for one month or less were considered to be naïve to therapy.

NUTRITIONAL STATUS ASSESSMENT

Nutritional status was assessed by: a) anthropometry; b) bioelectrical impedance analysis; and c) dietary intake.

Anthropometric measurements considered were weight, height, triceps skinfold (TSF), waist circumference (WC), hip circumference, body mass index (BMI), arm muscle area (AMA), and waist to hip ratio (W/H ratio). To quantify unintentional recent weight loss (if this information was not available from clinical records), subjects were asked about their weight history in the previous month. Weight was measured to the nearest kg with patients wearing light clothes and on bare foot using a calibrated scale, height to the nearest millimeter using a stadiometer, skinfold to the nearest 0.2 millimeter using a Harpenden caliper, WC and hip circumference to the nearest millimeter using a non-elastic measurement tape. TSF was measured at the mid-point between the acromion and the tip of the olecranon; WC, between the lowest rib and the iliac crest; and hip circumference, at the level of the anterior superior iliac spine at the end of a normal expiration. Male and female subjects with a WC ≥ 94 cm and ≥ 80 cm, and a W/H ratio ≥ 0.90 cm or ≥ 0.85 cm, respectively, were considered at risk for metabolic complications (15). Frisancho's data (16) were used as references for TSF and AMA measurements. TSF and AMA were considered in terms of their (%) adequacy, obtained according to the following formula (17): *TSF or AMA adequacy (%) = TSF obtained (cm) or AMA calculated (mm)* x *100/50th percentile of TSF or AMA*. Values ≥ 110% were considered as more

than adequate measurements; 90-110%, as adequate; and a measurement < 90% was considered as lower than adequate. Since Frisancho's data is derived from a Caucasian population, a second analysis, excluding black subjects was performed when these variables were used.

Bioelectrical impedance analysis was performed using a single-frequency analyzer (OMNRON BF350) to assess body fat percentage, and visceral fat; cut-off points for both measurements were used to classify the data (18,19).

To estimate *dietary intake,* a semi-quantitative Food Frequency Questionnaire (FFQ), validated for the Portuguese population, was used (20). The intake of macronutrients and micronutrients was analyzed continuously and in categories of intake to understand the adequacy of subjects' nutrient intake; this was done for protein, calcium, iron, water soluble and fat-soluble vitamins. The following formula was used to calculate nutritional adequacy: % adequacy = (nutrient intake*100)/recommended daily allowance (RDA). Two designations were used to describe the adequacy of intake: inadequate (< 90% of requirements), and adequate/more than adequate (≥ 90% of requirements). Adequate intakes for protein were ≥ 1.2 g/kg/day. Adequate energy intakes were those within 25-35 kcal/kg/day and inadequate, those above or below the 25-35 kcal/kg range (21).

LABORATORY DATA

Only results that had been collected in the 30-day period prior to the assessment were considered. The following were collected: blood pressure, lymphocyte CD4 and CD8 count, viral load, hemoglobin, lipid profile, fasting glucose concentration, liver and kidney function tests, total proteins, albumin, C-reactive protein (CRP), blood serum concentrations of ions. CD4 count was divided into three categories, according to the Centers for Disease Control (22).

QoL ASSESSMENT

The Portuguese version of the WHO Quality of Life Questionnaire (WHOQOL- HIV-BREF) was used to assess the QoL of the study population (23). The psychometric properties of the questionnaire have been validated for its use in Portuguese people living with HIV. The instrument contains six domains to assess QoL: physical health, level of independence, psychological health, social relations, environmental health, and spirituality. Thirty-one items are used to construct the six domains. There is also a general facet (General QoL), composed of two items, which examines QoL and health, in general (Q1 and Q2). All items are rated on a 5-point Likert scale; scores are scaled in a positive direction, where higher scores suggest a better QoL. Mean score of items in each domain were used to obtain the domain score. After computed, domain scores were transformed to a 0-100 scale to allow for comparison with the WHOQOL-100 instrument. The instrument's Users' Manual was used to score, code, check and clean data.

STATISTICAL ANALYSIS

The data collected was processed and analyzed using the IBM® SPSS® software, version 21. The internal consistency of the QoL instrument was measured with Cronbach's alpha. Descriptive statistics such as mean and standard deviation were used to summarize continuous data, and frequencies and proportions were used to summarize categorical variables. Parametric and non-parametric tests were used depending on variable distribution. Student's t-test and analysis of variance (ANOVA) were used to investigate differences in mean QoL scores of dichotomous variables, and variables with more than two groups, respectively. The level of significance was set at $p < 0.05$ in this study. Relevant variables that were found to be significantly related ($p < 0.05$) with QoL in bivariate analysis were subjected into multivariable analysis using a stepwise forward model building strategy to understand the effect that each significant independent variable had on the association nutrition-QoL, with other independent variables remaining constant. Outliers were excluded in multivariate analysis.

ETHICAL AND DEONTOLOGICAL CONSIDERATIONS

Ethical conditions were followed according to the Declaration of Helsinki, which ensured the informed voluntary participation and confidentiality of patient's data. The permission to gather information from patients registered at the hospital was obtained for a period of 12 weeks (starting on the 4th of January, 2016) by the director of the infectious diseases department. The study followed the hospital's protocols with regard to access to medical records.

RESULTS

STUDY SAMPLE

There were 191 patients who visited the outpatient clinic for the first time in 2015; 20 were excluded before screening because they were identified in advance as having tested positive for HIV before November 2014, elsewhere. Considering the remaining 171 potential eligible subjects in a year, a minimum of 43 subjects would need to be included to be representative of the study period (12 weeks starting on the 4th of January, 2016). During the 12-week study period, 53 subjects were screened; one subject was excluded because he was deaf, and another refused to participate due to time constraint. Fifty-one subjects met the inclusion criteria for the study and were enrolled.

STUDY SAMPLE CHARACTERISTICS: SOCIODEMOGRAPHIC AND CLINICAL DATA

Patient characteristics are illustrated in table I. Mean age was 41.1 years (± 14.2; range 21-74). Eleven subjects (21%) were

Table I. Sociodemographic and clinical data

Socio demographic/Clinical variable	n (%)
Gender	
Male	38 (74.5)
Female	13 (25.5)
Race	
Caucasian	38 (74.5)
Black	13 (25.5)
Literacy	
< Secondary	21 (41.2)
Secondary	6 (11.8)
Tertiary	19 (37.3)
Marital status	
Single	31 (60.8)
Married/In a relationship	18 (35.3)
Physical activity	
Yes	16 (31.4)
No	35 (68.6)
Employment	
Working	31 (60.8)
Not working	20 (39.2)
Current problem	
Yes	11 (21.6)
No	40 (78.4)
Hospitalized in the last year	
Yes	16 (31.4)
No	35 (68.6)
Medical history	
Yes	31 (60.8)
No	20 (39.2)
Other medication	
Yes	23 (45.1)
No	28 (54.9)
CD4 count	
< 350	17 (33.3)
> 350	34 (66.7)
CD4/CD8 ratio (mean)	
> 1	7 (13.7)
< 1	44 (86.3)
Viral load	
Detectable	28 (54.9)
Undetectable	22 (43.1)
Opportunistic infection	
Yes	10 (19.6)
No	41 (80.4)
HIV year diagnosis	
2014	10 (19.6)
2015	35 (68.6)
2016	5 (9.8)
Infection route	
Heterosexual	35 (68.6)
MSM	16 (31.4)
HAART	
Yes	30 (58.8)
Naive	21 (41.2)
Single tablet HAART regimen	
Yes	6 (11.8)
No	24 (47.1)

experiencing a current health problem; four had cancer (prostate, endometrial, Burkitt's lymphoma, Kaposi sarcoma), and the others ranged from heart failure, rheumatic disease, osteomyelitis. More than half of patients had a past medical history (60%), such as diabetes (5.9%), hypertension (3.9%), hepatitis B or C (11.8%), cancer (7.8%), syphilis (7.8%) and respiratory infection (3.9%). The remaining included uveitis, asthma and heart failure (opportunistic infections not included here). Almost half the patients (45.0%) were taking some kind of medication besides HAART such as sleeping pills, antidepressants, antibiotics, oral antidiabetic medication, antihypertensive drugs, or oral chemotherapy.

The mean CD4 and CD8 cell count was 522 cells/mm^3 (± 351; range 11-1,899) and 1,068.6 cells/mm^3 (± 638; range 113.5-2,942.0), respectively. The majority of patients (86%) had an inverted CD4:CD8 ratio (< 1). More than half had detectable viral loads (54.0%), and were under HAART (58.0%). The mean duration (in months) since HAART initiation was 7.8 months (± 4.5; range 1-19), and six patients (11.8%) were on a single tablet regimen. HIV diagnosis took place in 2015 for most patients (68.6%). The majority (47.0%) had been either infected in the year prior to assessment (2015) or they did not know when it happened (39.2%), and the remaining, had been infected in 2014 (13.7%). Ten patients (20.0%) had experienced an opportunistic infection in the past. In one third of patients (31.4%) HIV transmission occurred in men who had sex with men (MSM).

NUTRITIONAL STATUS ASSESSMENT

Subjects' anthropometric, body composition and nutrient intake data are illustrated in table II. One patient was underweight, according to BMI, most were normal weight (60.8%), and more than one third (37.3%) were overweight or obese. TSF and AMA were lower than adequate for 66.7% and for 33.3% of the sample, respectively. According to WC and W/H ratio, 20 (39.2%) and 16 (31.4%) subjects had a high metabolic risk, respectively. A similar proportion of patients had a healthy and a high body fat mass (41.2% and 47.1%, respectively), and the visceral fat of four subjects (8.0%) was above the ≥ 12% reference cut-off value (22). Only 25.5% of patients had adequate energy intakes (25-35 kcal/kg). Protein intakes were adequate for most subjects (82.4%). Folate and biotin intakes were inadequate for more than half of the study sample and one quarter had inadequate pantothenic acid intakes. Less than five individuals (9.8%) had an inadequate intake of one or more of the remaining water-soluble vitamins (data not reported). Over 80% of the sample had inadequate intakes of vitamins D, E, and K. Vitamin A was the exception, where intakes were adequate for all, but two individuals.

LABORATORY DATA

Data was not available for every biomarker of each of the 51 patients. Total cholesterol, LDL-c HDL-c, and triglycerides were measured in 31-35 individuals; 25.0% had levels above the ref-

Table II. Nutritional status of study sample

Nutritional parameter	n (%)
BMI (kg/m²)	
Normal weight	31 (60.8)
Overweight/obese	19 (37.3)
Waist Circumference (cm)	
Risk	20 (39.2)
No risk	29 (56.9)
W:H ratio	
Risk	16 (31.4)
No risk	32 (62.7)
% Adeq TSF thickness	
Lower than adequate	34 (66.7)
Adequate	6 (11.8)
≥ Adequate	11 (21.6)
% Adeq AMA	
Lower than adequate	17 (33.3)
Adequate	10 (19.6)
≥ Adequate	24 (47.1)
Fat mass (%)	
Under fat	5 (9.8)
Healthy	21 (41.2)
Over fat	24 (47.1)
Visceral fat (%)	
> 12%	4 (7.8)
< 12%	45 (88.2)
Weight loss ≥ 1 kg	
Yes	14 (26.9)
No	21 (40.4)
Energy (kcal)	
Inadequate	38 (74.5)
Adequate (25-35 kcal/kg)	13 (25.5)
Protein (g)	
Inadequate	9 (17.6)
≥ Adequate	42 (82.4)
Folate (µg)	
Inadequate	16 (31.4)
≥ Adequate	35 (68.6)
Vitamin A Tot (µg)	
Inadequate	2 (3.8)
≥ Adequate	49 (94.2)
Vitamin D (µg)	
Inadequate	51 (100)
≥ Adequate	0 (0)
Vitamin E (mg)	
Inadequate	44 (84.6)
≥ Adequate	7 (15.4)
Vitamin K (µg)	
Inadequate	50 (98.1)
≥ Adequate	1 (1.9)

BMI: Body mass index; W:H: Waist:hip.

erence interval for total cholesterol, 78.8% were not within the reference range for HDL-c, only one individual had an abnormal LDL-c, and 17.6% had elevated triglycerides. Hepatic function indicators, ALT, AST, GGT, and bilirubin levels were measured in 39, 47, 31, and 34 subjects, respectively; less than half of subjects had inadequate levels of any one of these biomarkers. Hemoglobin was within a healthy range for 26 (63.0%) individuals out of a total of 41 measured. From the 43 values available for blood glucose, eight subjects (18.6%) had elevated levels. Other biomarkers such as total proteins, albumin, kidney function, were not considered as relevant since they were only available for a small number of individuals (< 14).

QUALITY OF LIFE

The internal consistency of the WHOQOL-HIV-BREF using Cronbach's alpha coefficient, was > 0.7 for all six domains, and for General QoL, it was 0.6. Table III illustrates patient's mean QoL scores for each domain and for general QoL. When considering the mean scores of all subjects, the lowest scores observed were those for general QoL (61.3 ± 18.8), followed by physical health (63.2 ± 21.5). The highest scores were observed for the level of independence (72.1 ± 20.2).

SOCIODEMOGRAPHIC AND CLINICAL DATA

Table III illustrates results from bivariate analysis of sociodemographic, clinical and nutritional data with QoL. Gender, education level, infection route, current health problem, and physical activity were shown to be significantly different across three or more QoL dimensions. Significant differences in QoL according to education level were only observed between individuals without secondary education, and those with a tertiary level of education, after multiple comparison tests. QoL scores were significantly different across the different employment, race, medical history, transmission mode and CD4 lymphocyte categories in one or two dimensions. The significant differences observed in CD4 lymphocyte count were between the lowest and highest class. Age was negatively and significantly correlated to the level of independence ($r = -0.3$, $p = 0.028$). No other significant differences in QoL scores across the different sociodemographic (marital status/relationship) or clinical variables (hospitalized in the last year, HAART status, duration of infection, duration of HAART, viral load, history of opportunistic infections, HAART single-tab regimen, CD4/CD8 ratio) were observed.

NUTRITIONAL STATUS AND QoL

The QoL of patients, according to nutritional status, is illustrated in table III. There was only one subject who was underweight, and he was excluded when testing BMI. Only two classes were compared (normal weight and overweight/obesity).

Table III. Mean QoL scores by sociodemographic, clinical and nutritional status

	Mean QoL domain score (SD)						
	General QoL	**Physical health**	**Psychological health**	**Level of independence**	**Social relationships**	**Environment**	**Spirituality**
Mean QoL	61.3 (18.8)	63.2 (21.5)	69.2 (18.4)	72.1 (20.2)	67.6 (19.3)	69.1(16.8)	66.3 (23.7)
Gender							
Female	49.0 (16.5)**	54.2 (19.3)**	60.8 (20.9)	61.4 (22.7)*	56.9 (18.0)*	58.9 (11.8)*	58.7 (20.8)
Male	65.4 (17.8)	66.1 (21.6)	71.9 (16.9)	75.6 (18.4)	70.8 (18.7)	72.5 (16.9)	69.3 (24.4)
Race							
Caucasian	65.2 (17.7)*	65.1 (20.8)	70.3 (18.2)	73.6 (18.6)	69.4 (19.3)	71.3 (16.1)	66.7 (24.1)
Other	50.0 (17.7)	57.3 (23.5)	65.8 (18.6)	66.9 (25.7)	61.3 (18.6)	62.5 (17.6)	65.4 (23.6)
Level of education							
< Secondary	53.0 (19.3)**	52.2 (19.2)**	64.5 (21.3)	60.2 (21.1)**	63.5 (23.1)	64.2 (16.2)*	63.4 (23.9)
Secondary	58.3 (15.1)	65 (14.4)	65.0 (12.2)	79.2 (13.0)	64.1 (13.9)	58.1 (14.8)	73.4 (21.3)
Tertiary	73.6 (14.1)	75 (17.9)	76.1 (15.8)	84.3 (9.6)	72.4 (15.9)	78.5 (16.5)	68.3 (25.7)
Physical activity							
Yes	71.9 (15.5)**	75.4 (16.8)**	74.1 (21.8)	81.6 (14.2)*	74.6 (20.8)	76.8 (17.0)*	80.0 (27.1)
No	56.3 (18.3)	57.0 (21.2)	66.7 (16.2)	66.8 (21.3)	64.0 (17.7)	65.2 (15.4)	64.2 (22.2)
Employment							
Working	64.6 (16.8)	66.7 (19.5)	71.6 (19.4)	77.0 (16.9)*	67.5 (21.7)	72.3 (16.4)	67.5 (21.6)
Not working	56.3 (20.9)	58.1 (23.6)	65.8 (16.7)	64.0 (23.0)	67.7 (15.6)	64.5 (16.6)	64.7 (24.6)
Current problem							
Yes	48.9 (17.2)*	43.1 (19.1)*	59.5 (21.1)*	49.3 (21.8)*	56.9 (17.0)*	58.5 (14.7)*	55.7 (17.8)
No	64.7 (17.9)	69.0 (18.6)	72.0 (16.8)	77.8 (15.5)	70.7 (19.0)	72.2 (16.2)	69.6 (24.6)
Medical history							
Yes	58.5 (18.9)	57.1 (22.1)*	66.9 (20.1)	66.7 (22.3)*	66.7 (19.5)	67.3 (17.9)	63.3 (23.8)
No	65.8 (18.1)	74.3 (15.6)	73.2 (14.6)	80.9 (12.4)	69.1 (19.4)	72.2 (14.4)	71.9 (23.4)
Transmission mode							
Heterosexual	58.2 (17.9)	62.1 (21.0)	66.5 (18.9)	69.2(20.2)	64.6(19.8)	65.4 (16.6)*	62.5(62.5)
MSM	68.3 (19.4)	65.6 (23.2)	75.7 (15.9)	78.6 (19.4)	74.1 (17.0)	77.9 (13.9)	77.1 (77.1)
CD4 count							
≥ 500	63.0 (17.1)	68.5 (20.0)	70.5 (17.9)	78.4 (15.0)*	65.3 (19.5)	70.0 (15.8)	64.5 (24.3)
200-499	59.4 (19.1)	57.0 (21.8)	64.7 (16.2)	67.2 (19.7)	68.4 (19.0)	69.9 (15.9)	65.8 (24.0)
< 200	58.3 (24.2)	59.1 (23.8)	71.7 (23.5)	57.3 (28.6)	70.5 (22.2)	62.5 (19.8)	68.0 (23.0)

(Continue in the next page)

Table III (Cont.). Mean QoL scores by sociodemographic, clinical and nutritional status

	Mean QoL domain score (SD)						
	General QoL	**Physical health**	**Psychological health**	**Level of independence**	**Social relationships**	**Environment**	**Spirituality**
Waist circumference							
Risk	51.3 (18.6)*	58.5 (22.2)	64.1 (20.4)	66.9 (23.4)	62.9 (22.2)	65.6 (17.5)	61.4 (25.6)
No risk	67.2 (16.8)	66.8 (20.7)	72.4 (17.4)	75.9 (17.7)	70.9 (17.7)	71.2 (16.8)	69.9 (23.2)
% Adeq AMA							
Lower than adequate	67.6 (15.3)	64.7 (19.4)	78.2 (10.4)*	76.3 (14.3)	74.2 (15.0)*	73.2 (15.5)	69.5 (21.5)
Adequate	62.5 (13.2)	65.0 (22.7)	72.0 (14.8)	76.3 (18.4)	71.9 (14.5)	73.1 (16.2)	69.5 (23.3)
≥ Adequate	56.0 (21.9)	61.0 (23.4)	60.5 (21.4)	67.3 (23.9)	60.2 (22.5)	63.8 (17.3)	62.5 (26.1)
Weight loss ≥ 1 kg							
Yes	57.1 (22.3)	54.5 (26.1)	60.7 (23.1)*	64.9 (28.5)	65.9 (22.0)	62.7 (22.0)	62.9 (28.1)
No	63.8 (20.6)	69.8 (19.0)	78.3 (16.2)	75.0 (15.8)	70.6 (20.8)	72.4 (15.5)	71.9 (23.6)
% Adequacy energy intake							
Not adequate	57.8 (17.0)*	61.4 (19.9)	67.9 (18.3)	70.1 (19.0)	66.2 (19.9)	67.4 (17.7)	63.8 (24.9)
Adequate	71.2 (20.7)	67.8 (25.7)	72.7 (19.0)	76.9 (22.9)	71.4 (17.7)	73.6 (13.4)	74.4 (18.0)

Social RS: Social relationships; QoL: Quality of life; HET: Heterosexual; MSM: Men sex with men; AMA: Arm muscle area. **Significant at 95% CI, p value < 0.05. **Significant 99% CI, at p value < 0.01. Only variables with significant differences in one or more QoL dimensions are presented.*

No significant differences in QoL scores were observed across the different categories of BMI, % TSF adequacy, W/H ratio, % body fat, and protein intake. As a continuous variable, % body fat was inversely associated with general QoL ($r = -0.4$, $p = 0.010$), psychological health ($r = -0.3$, $p = 0.043$), and borderline significantly associated with level of independence ($r = -0.3$, $p = 0.064$). Significant differences in QoL scores were found across the different categories of waist circumference, % AMA adequacy, unintentional weight loss, and energy intake (Table III). The mean psychological domain score was significantly different across the three different AMA classes (lower than adequate, adequate, more than adequate); a second analysis, comparing the lower and higher AMA class, showed that the difference remained significant in the psychological domain, and in addition, became significant in the social domain, where higher QoL scores were observed in the lower (lower than adequate) AMA class. Excluding black subjects from analysis did not affect the results of the variables using reference percentiles for Caucasians. As a continuous variable, % AMA was correlated with general QoL ($r = 0.3$, $p = 0.033$), psychological health ($r = -0.4$, $p = 0.010$), and social relationships ($r = -0.3$, $p = 0.042$). QoL scores across the different energy intake categories are shown in table III. The 13 subjects with adequate energy intakes (25-35 kcal/kg) rated their general QoL significantly higher compared to subjects with inadequate intakes. Individuals consuming ≥ adequate protein intakes, compared to those with inadequate intakes, did not differ significantly in QoL scores. Only two individuals had inadequate iron intakes and therefore results were not considered to be relevant (data not shown). Vitamin K and D intakes were not tested for the same reason. The correlations with other micronutrients were not significant (data not show). Higher alcohol intakes were associated to significant lower scores in environmental health ($r = -0.3$, $p = 0.028$).

LABORATORY RESULTS AND QoL

Hemoglobin level was significantly correlated to general QoL ($r = 0.4$, $p = 0.013$), physical health ($r = 0.5$, $p < 0.001$), psychological health (0.4, $p = 0.027$), level of independence ($r = 0.5$, $p = 0.001$), social health ($r = 0.4$, $p = 0.011$), and environmental health ($r = 0.4$, $p = 0.028$). CRP (only analyzed 14 patients) correlated moderately with the level of independence ($r = -0.5$, $p = 0.157$). AST correlated negatively and significantly with physical health ($r = -0.4$, $p = 0.023$). The remaining biochemical biomarkers measured did not correlate significantly with QoL and were not reported.

MULTIVARIATE ANALYSIS

Variables that were significant in bivariate analysis (age, gender, race, employment status, education level, medication, medical history, current health problem, CD4 count, % AMA, weight loss that was unintentional, WC, energy intake, alcohol intake, hemoglobin) were subjected into multivariate analysis. Table IV illustrates the results of the multivariate analysis. The regression model explained between 31.0% and 52.2% of the variance in the different domains. No significant predictor for the spiritual domain was identified. After adjusting for the different confounders, inadequate energy intakes, an unhealthy WC, a ≥ adequate AMA (*versus* lower than adequate), and unintentional weight loss were found to be significantly associated with lower QoL scores. WC and energy intake were the strongest determinants of general QoL. A lower % AMA adequacy and weight loss were the strongest determinants of psychological health. Energy was associated with general QoL ($p < 0.01$), and level of independence ($p = 0.025$); weight loss was associated with psychological ($p = 0.02$) and environmental health ($p < 0.01$). In multivariate analysis, physical activity only predicted QoL in social relationships, hemoglobin predicted social relationships and physical health ($p < 0.05$), and non-antiretrovial medication predicted patients' level of independence ($p < 0.05$). Education and current health problems influenced most of the QoL domains significantly.

DISCUSSION

As far as our knowledge extends, this is the first study investigating the relationship between nutritional status and QoL in HIV-infected individuals in Europe. QoL is affected by culture and level of economic development, which explains why developing countries report poorer QoL outcomes compared to developed countries; as a result, extrapolation of other studies findings must be carefully made. Although the relationship between HIV and malnutrition has been studied, few have looked at QoL as a consequence of the synergy between these two (1,11-13). This study involved 51 subjects with a relatively recent HIV diagnosis; the majority were Caucasian, male, employed, and had finished secondary school. More than half were under HAART, of which more than one third had detectable viral loads. Compared to the QoL of participants enrolled in the validation of the Portuguese WHOQOL-HIV-BREF, with the exception of physical health, the scores of all QoL dimensions were higher in this sample, independent of disease stage (23). Our study only involved patients with a recent HIV diagnosis, which probably explains the better QoL outcomes compared to the former study, since patients with an advanced stage of the disease present a lower QoL (24). In line with most studies reporting gender inequalities in QoL in this population (25), men reported higher scores in QoL compared to women across most dimensions, although in multivariate analysis gender was only associated with environmental health. Consistent with previous research (26,24), the present findings indicate that subjects with higher education have an enhanced QoL across all domains, compared to those who did not complete secondary education. A higher education and income have been associated to better coping strategies (24), which may explain the difference in scores. Similar to previous findings (27), this study did not detect significant differences in QoL among subjects who were married/in a relationship, compared to single subjects. In this study MSM were significantly more satisfied

Table IV. Multivariate analyses: linear regression models to identify QoL predictors

Independent predictors for each dependent variable	Beta	R^2_a	F	p-value
General QoL		52.2%		
WC	-13.629		12.242	0.001
Energy	13.158		9.699	0.003
Education	-11.998		9.141	0.004
Current problem	-8.367		3.046	0.088
Physical health		31.0%		
Education	-12.695		6.331	0.016
Hb	3.924		5.811	0.020
Current problem	-12.949		4.240	0.046
Medical history	-10.066		4.068	0.050
Psychological health		32.2%		
AMA	13.972		11.119	0.002
Weight loss	-11.739		5.652	0.022
Education	-9.267		4.687	0.036
Level of independence		57.5%		
Education	-13.943		12.838	0.001
Current problem	-16.028		9.240	0.004
Medication	-10.542		7.191	0.011
Energy	9.707		5.497	0.025
Social relationships		55.5%		
Physical activity	12.899		10.220	0.003
Hb	3.899		9.601	0.004
Age	-0.248		4.404	0.045
Environment		50.9%		
Gender	-11.236		10.304	0.003
Weight loss	-12.918		9.677	0.004
Education	-9.598		8.119	0.007
Spirituality	No significant predictor identified			

with their environment compared to heterosexuals; this could be related to the social support groups they are part of, which have shown to be inversely related to rates of depression (28). Patients who were currently ill reported significant lower scores in various domains, which is consistent with most QoL-related works in HIV subjects (29,30). Although evidence is conflicting, significant differences among QoL domains with stages of HIV infection have been reported (12,24); similarly, in this study, the level of independence was significantly superior in subjects with CD4 counts > 500 compared to those with < 200. Despite the absence of significance, patients under HAART had worst QoL outcomes compared to naïve-treatment patients. This finding is in agreement with results of a cross-sectional study (24) where lower scores in all domains were observed in patients in the first year of HAART, compared to naïve patients; the QoL of those who were being treated for more than one year, however, was better than for those in the first year of treatment, and this has been documented elsewhere too (12). Again, despite the absence of significance, those under HAART for a longer time had higher QoL scores across all domains compared to subjects under treatment for a shorter period. This could be related to the side effects of treatment experienced at the start of HAART (12). Patients switching to a HAART single-pill fixed dose regimen in an Italian trial experienced non-significant improvements in QoL (29); in the present investigation QoL was better in subjects on a single-pill regimen ($p > 0.05$). The present study reports improved QoL scores for patients who were physically active compared to those who were not, in most dimensions. Physical activity and nutrition counselling contributed to significant improvements in QoL, nutritional status and clinical parameters in a trial (31) and

in another study moderate physical activity was associated with physical, psychological and immunological benefits (32).

This study did not find significant variations in QoL with BMI class, in contrast to other works involving HIV patients (1,11,12). However, only two classes of BMI were compared, due to the absence of underweight and obese class I-III subjects enrolled in the study. The poor psychological outcome observed in patients with unintentional weight loss in this study is in agreement with former findings (24). The fact that weight loss is an important marker of disease progression and symptom status may help explain these results. Also, alterations in body image significantly impact on psychosocial wellbeing and QoL (33), suggesting different aspects influencing psychological outcome.

In this study, a moderate-high WC was a significant contributor to a worst outcome in general QoL; this is strongly associated to a poor QoL (34). Exercise has been shown to reduce WC in HIV-patients (35); therefore, there may be a role for exercise as a potential strategy to improve nutritional status and, consequently, QoL (31,35). In contrast to the limited available evidence on AMA and QoL suggesting a positive relationship between the two (36), an inverse relationship was found in the present study, where the lowest QoL scores were observed in subjects with ≥ adequate AMA measurements (though similar scores were observed for lower than adequate and adequate categories). Heymsfield et al. (37) showed that the equation for calculating AMA overestimated it by 25%; this could mean that part of the subjects who were found to exceed AMA adequacy (47.1%) in this study could actually have adequate measurements, and this could have led to the confusing interpretation of results. In this study, lower QoL scores, particularly in general QoL and psychological health, were observed in subjects with higher body fat percentages. The association between body fat percentage and QoL in this population has not been well documented to date, but higher percentages of body fat were associated to lower QoL scores observed in other chronic disease patients (38).

When weight maintenance is the goal, energy requirements should match energy expenditure; however, the latter is poorly understood in chronic disease such as HIV (39). In this study, intakes ranging 25-35 kcal/day were considered as normal and subjects within this range of intake had better QoL outcomes for general QoL.

Biochemical markers did not play a significant role in predicting QoL in this study with the exception of hemoglobin. The strong correlations found are consistent with previous findings (40) where improvements in hemoglobin translated into significant improvements in QoL.

Deterioration in nutritional status and the associated changes in muscle, immune, and cognitive function observed in other populations (41) probably explain the decline in physical, mental, and environmental performance observed in this work and others investigating nutrition and QoL. Similar to the present work, which reports nutritional status to explain over one third of the variance in QoL, regression analysis in other works with chronically ill patients determined that > 25% of the variation change in QoL was explained by changes in nutritional status (38,42). Correcting the energy density of the diet, becoming physically active, achieving a healthy body composition, and preventing unintentional weight loss could lead to improvements in QoL, according to the findings reported in this study.

STRENGTHS AND LIMITATIONS

Despite the small number of individuals enrolled in this study, all nutritional parameters associated with QoL in bivariate analysis remained significant in multivariate analysis, implying that different aspects of nutritional status are likely to have a reasonable impact on different QoL dimensions. Due to the heterogeneous characteristics of HIV patients, this study only focused on patients with a recent HIV diagnosis to prevent further confounding of the data. This means that findings should carefully be extrapolated to the different stages of HIV infection.

Although the use of a FFQ relies on long-term memory and does not take into account the intake of foods from different ethnic/racial groups, a population validated FFQ was used in this work; other methods are unable to describe the usual diet, or are very time consuming.

Although the occurrence of physical activity was recorded, details on the nature of the exercise performed could have helped understand the type of exercise necessary to achieve beneficial outcomes in QoL.

Accurate individual nutritional requirements are dependent on stage of infection, HAART status, nutritional status, HIV-related symptoms, and many others. Equations to calculate energy requirements were not used since activity factors were not recorded. By establishing a large range of adequate energy intake (25-35 kcal/kg), or a minimum adequate intake for protein (1.2 g/kg), with the intention to cover the requirements of all individuals, is not sufficiently accurate to determine how far requirements are being met.

CONCLUSION

This study found worst QoL outcomes with inadequate energy intakes, presence of unintentional weight loss, and a moderate-high waist circumference. QoL was higher in subjects undergoing physical activity. Despite clinical and sociodemographic patient characteristics having shown to be significant predictors of QoL in this population, with advances in HIV treatment and prolonged survival times, finding strategies to maximize QoL such as integrating nutrition advice and exercise into HIV-treatment plans could serve as simple, cost-effective tools with the potential to improve or prevent the occurrence of events that have been shown to deteriorate QoL. More studies involving on-going nutritional and QoL assessment in HIV patients are required to understand the long-term impact therapeutic, dietary and lifestyle modifications have on the different QoL dimensions in this chronically-ill population.

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