

Anthropometric and Quality-of-Life Parameters in Acute Intermittent Porphyria Patients

Antonia M Jiménez-Monreal, PhD, M Antonia Murcia, PhD, Victoria Gómez-Murcia, Maria del Mar Bibiloni, PhD, Antoni Pons, PhD, Josep A. Tur, PhD, and Magdalena Martínez-Tomé, PhD

Abstract: The porphyrias are a group of rare metabolic disorders. The incidence and prevalence are low because the acute intermittent porphyria (AIP) is rare. Our aim was to assess the use of anthropometric and quality-of-life parameters in porphyric patients in order to identify predictor factors that might help in characterizing AIP patients.

Sixteen AIP patients from Murcia (Spain) were recruited from local health centers in 2008 and 2009. A control group of 16 healthy people was established. Body composition was assessed by bioelectrical impedance analysis (BIA) and anthropometric measurements: body weight; height; knee-heel height; waist, hip, upper arm and calf circumferences (CCs); biacromion and biiliac diameters; bicondylar and bipicondylar width; and triceps, subscapular, supraspinale, and calf skinfold thickness. Anthropometric indicators were obtained from anthropometric measurements. A quality-of-life evaluation was carried out using the EuroQol-5D (EQ-5D) questionnaire and Barthel and Katz indexes. Significant differences in means were tested by unpaired Student *t* test. Group differences in anthropometric measurements were tested with a 2-way analysis of variance (group $\times$ condition: age group, overweight, and adiposity degree). Relative frequencies were obtained for noncontinuous variables. Significant differences in prevalence were calculated by means of χ^2 .

AIP patients showed statistically significant differences in terms of knee-heel height, biiliac diameter, CC, triceps skinfold thickness, BIA, ponderal index, endomorphy, and ectomorphy. Only 1 quality-of-life indicator, visual analog scale, in the EQ-5D questionnaire showed significant differences between porphyric and control groups.

Some anthropometric parameters and the EQ-5D questionnaire could be used to appreciate the presence or follow the evolution of the disease in AIP patients.

(*Medicine* 94(30):e1023)

Abbreviations: ADL = activities of daily living, AIP = acute intermittent porphyria, BIA = bioelectrical impedance analysis, BMI = body mass index, CC = calf circumference, EQ-5D = EuroQol-5D, HRQoL = health-related quality of life, HWR = ponderal index, MAC = midarm circumference, PBGD = porphobilinogen deaminase, TE = temporal equivalence, VAS = visual analog scale.

INTRODUCTION

Porphyrias are a group of 8 inherited metabolic disorders of heme biosynthesis. Acute intermittent porphyria (AIP) is caused by catalytic deficiency of porphobilinogen deaminase (PBGD), the third enzyme in heme biosynthesis. This pathology is estimated to affect about 1 in 75,000 people in European countries, and is endemic in the province of Murcia, Spain.^{1,2} Its incidence and prevalence are low because AIP is rare. AIP is usually diagnosed when patients show symptoms of an acute attack but its confirmation may depend on measuring urinary porphyrin precursors, in combination with PBGD activity.² Therefore, making a precise diagnosis is difficult although it is well known that AIP is frequently associated with chronic under nutrition,³ meaning that an evaluation of nutritional status is important for early diagnosis. Several noninvasive methods exist for such an evaluation, including anthropometry, which provides detailed information on the different components of the body structure, especially muscular and fat components, which can be used to obtain the nutritional indices.⁴ The association of anthropometric indices with lifestyle-related chronic diseases has been the subject of intensive investigation in recent years. Anthropometry has been included in nutritional assessment and screening scales, many of which have been shown to predict functional decline, morbidity, and follow-up mortality risk.⁵

Other methods have been described that relate malnutrition with quality of life.^{6,7} Indeed, the measurement of health-related quality of life (HRQoL) is an essential component in the overall assessment of the health status of adult subjects, as it represents people's subjective assessment of their sense of well-being and their ability to perform social roles.⁸ In this respect, the EuroQol-5D (EQ-5D) is a generic health assessment instrument, which has shown good internal consistency when applied to the general population and to groups of patients with various diseases.⁹

The activities of daily living (ADL) are the main focus of the measurements of health and quality of life. Among the instruments of ADL, the Barthel and Katz indexes, which systematically evaluate the functional status as a measurement of the patient's ability to perform ADL independently, have become standards.¹⁰

Editor: Sanket Patel.

Received: February 11, 2015; revised: May 8, 2015; accepted: May 26, 2015.

From the Department of Food Science (AMJ-M, AM, VG-M, MM-T), Regional Campus of International Excellence "Campus Mare Nostrum," University of Murcia, Murcia; CIBEROBN (Fisiopatología de la Obesidad y la Nutrición CB12/03/30038) (AMJ-M, AM, MMB, AP, JAT, MM-T), Instituto de Salud Carlos III, Madrid; and Research Group on Community Nutrition and Oxidative Stress (MMB, AP, JAT), University of the Balearic Islands, Palma de Mallorca, Spain.

Correspondence: Magdalena Martínez-Tomé, Department of Food Science, Faculty of Veterinary, University of Murcia and CIBEROBN CB12/03/30038, Campus of Espinardo 30100, Murcia, Spain (e-mail: mmtome@um.es).

This study was funded by the Spanish Ministry of Health and Consumption Affairs (Programme of Promotion of Biomedical Research and Health Sciences, Project AGL2007-62806/ALI, Project 11/01791, Red Pre-dimed-RETIC RD06/0045/1004, and CIBEROBN CB12/03/30038) and EU FEDER Funds.

The authors have no conflicts of interest to disclose.

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

This is an open access article distributed under the Creative Commons Attribution-NonCommercial License, where it is permissible to download, share and reproduce the work in any medium, provided it is properly cited. The work cannot be used commercially.

ISSN: 0025-7974

DOI: 10.1097/MD.0000000000001023

Accordingly, the objective of the current study was to assess the use of anthropometric and quality-of-life parameters to identify factor predictors that might help to establish discriminator parameters in AIP patients.

MATERIALS AND METHODS

Subjects

A total of 32 subjects participated in this transversal descriptive observational study. Sixteen AIP patients (11 females and 5 males) with a mean age of 49.8 ± 4.2 years from Murcia, Spain, were recruited from local health centers in zones where the disease is endemic. Sixteen healthy subjects (11 females and 5 males) with a mean age of 48.6 ± 4.0 years were also enrolled in the study. These were selected according to 3 characteristics: similar age, height, and weight of the AIP patients. This study uses a reduced population because of the low incidence and prevalence of the disease, which is considered a rare disease. The study was approved by the Ethics Committee of the University of Murcia, and written informed consent was obtained from all subjects.

Anthropometric Measurements

The following methods or instruments were used to assess body composition: body weight was determined using a digital electronic scales (Seca 812, Hamburg, Germany); height using a digital stadiometer (Kawe, Asperg, Germany), with the subject's head in the Frankfurt plane; waist, hip, upper arm, and calf circumferences (CCs) using an inelastic tape (Seca 201, Hamburg, Germany); knee-heel height and biacromion and biiliac diameters using an anthropometer (GPM 101, Zurich, Switzerland); bicondylar and biepicondylar using a caliper (Mitutoyo 160–170 C20P, Japan), and triceps, subscapular, supraspinale, and calf skinfold thicknesses using a skinfold caliper (Holtain T/W, Crymych, UK). The body fat percentage was calculated by bioelectrical impedance analysis (BIA) (OMRON BF 306, Kyoto, Japan).^{11,12}

From the anthropometric measurements obtained, anthropometric indicators were calculated, among them body mass index (BMI) or Quetelet index, defined as the ratio between weight and the square of the height, is used in epidemiology as a universal index of nutritional status.¹³ According to the adiposity level, BMI is classified as normal ($\text{BMI } 20\text{--}24.9 \text{ kg/m}^2$), overweight ($\text{BMI } 25\text{--}29.9 \text{ kg/m}^2$), or obese ($\text{BMI } 30\text{--}34.9 \text{ kg/m}^2$).¹⁴ To calculate the corrected BMI value, we considered the corrected height, which, in turn, is obtained from the knee-heel height parameter by the equation described by Chumlea et al.¹⁵ The structural design (android/gynoid) determined by Tanner Score (calculated as the difference between 3 times the biacromion and biiliac diameters) provides information on cardiovascular protection, as it is related to estrogen levels, from which it follows that a gynoid structure provides greater protection than an android structure.¹⁶

The waist-to-hip ratio is the indicator most commonly used to predict visceral fat accumulation in epidemiological studies, defined as the ratio between waist and hip circumferences.^{17,18}

Body fat percentage is calculated from triceps and subscapular folds, from which the total body fat can be ascertained, where c and m are constants that vary depending on whether the measured subject is male or female and the type of fold measured (subscapular and triceps).

$$\text{Body fat (g/mL)} = c - m \times \log_{10}(\text{folds (mm)})$$

Arm muscular area (AMA) was calculated from midarm circumference (MAC) and triceps skinfold thickness.

From AMA, total muscle mass (TMM) can be obtained as follows:

$$\text{AMA (cm}^2\text{)} = \frac{\pi}{4} \left(\frac{\text{MAC (cm)}}{\pi} - \text{triceps fold thickness (cm)} \right)^2 - \text{Cte}$$

$$\begin{aligned} \text{TMM (kg)} &= \text{height (cm)} \\ &\times (0.024 + 0.0029 \times \text{AMA (cm}^2\text{)}) \end{aligned}$$

$$\text{TMM (\%)} = \frac{\text{TMM (kg)}}{\text{Weight (kg)}} \times 100$$

Finally, the somatotype is a composite estimate of body build. Three components, which together define the individual's physique, are not independent of each other, given that endomorphy reflects wide hips and narrow shoulders, a high level of body fatness, upper arms and thighs, and slim wrists and ankles; mesomorphy reflects broad shoulders and relatively narrow hips, a muscular body, strong forearms and thighs, very little body fat; finally, ectomorphy reflects narrow shoulders, hips and chest, thin face, high forehead, thin legs and arms, and very little muscle or fat. The formulas applied to calculate somatotype are the following¹⁹:

$$\begin{aligned} \text{Endomorphy} &= -0.7182 + 0.1451 \cdot \left(\sum \right) - 0.00068 \cdot \\ &\sum^2 + 0.0000014 \cdot \sum^3 \end{aligned}$$

$$\begin{aligned} \text{Mesomorphy} &= (0.858 \times \text{HB} + 0.601 \times \text{FB} + 0.188 \\ &\times \text{CAG} + 0.101 \times \text{CCG} - 0.131 \\ &\times \text{Height}) + 4.5 \end{aligned}$$

Ectomorphy:

If $\text{HWR} > 40.75$, then ectomorphy = $0.463 \times \text{PI} - 17.63$

If $\text{HWR} > 38.25$ and ≤ 40.75 , then ectomorphy = $0.732 \times \text{PI} - 28.59$

If $\text{HWR} \leq 38.25$, then ectomorphy = 0.1

where $\sum$ is the sum of triceps, subscapular and supraspinale skinfolds multiplied by $(170.18/\text{height in cm})$; HB is the humerus breadth (biepicondylar width); FB is the femur breadth (bicondylar width); CAG is corrected arm girth; CCG is corrected calf girth; and HWR is height/cube root of weight. CAG and CCG are the girths corrected for the triceps or calf skinfolds, respectively, as follows: CAG = flexed arm girth-triceps skinfold/10; CCG = maximal calf girth-calf skinfold/10.

Health-Related Quality-of-Life Questionnaires

The EQ-5D questionnaire measures HRQoL over 5 domains (physical, self-care, ability to perform usual activities, pain/discomfort, and anxiety/depression), generating a single profile of the individual's state of health. The HRQoL scoring system provides utility scores on a generic scale from worse than dead = 0.00 and perfect health = 1.00. The EQ-5D also includes a subjective evaluation of the subject's own health, the visual analog scale (VAS), on which the respondent is asked to mark his or her own current state of health on a thermometer-like line calibrated from 0 (worst imaginable health state) to 100

TABLE 1. Anthropometric Parameters for Acute Intermittent Porphyria Patients and Their Controls^{*,†}

	Porphyria (n = 16)	Control (n = 16)	P values
Age, y	49.75 (4.24)	48.63 (4.04)	0.85
Weight, kg	72.54 (2.68)	69.44 (2.68)	0.45
Height, cm	160.34 (2.14)	165.00 (1.76)	0.10
Knee-heel height, cm	51.96 (0.81)	48.70 (0.95)	<0.05
Body diameters			
Biacromial, cm	36.16 (0.72)	35.93 (0.70)	0.82
Biiliac, cm	32.71 (1.23)	29.33 (0.89)	<0.05
Biepicondylar width, cm	6.59 (0.25)	6.54 (0.15)	0.85
Bicondylar width, cm	9.28 (0.62)	9.63 (0.20)	0.60
Body circumferences			
Arm, cm	30.64 (0.77)	28.54 (1.04)	0.12
Flexed midarm, cm	32.52 (0.60)	30.53 (1.25)	0.16
Waist, cm	91.14 (3.00)	86.27 (2.79)	0.24
Hip, cm	105.82 (2.67)	102.10 (2.18)	0.29
Calf, cm	40.44 (1.47)	35.88 (0.68)	<0.01
Skinfold thicknesses and BIA			
Triceps, mm	25.14 (2.13)	17.64 (2.27)	<0.05
Subscapular, mm	22.76 (1.36)	19.86 (1.71)	0.19
Supraspinale, mm	26.68 (1.87)	22.11 (2.30)	0.13
Calf, mm	25.53 (2.21)	21.50 (3.07)	0.29
BIA, % fat mass	38.05 (1.94)	31.88 (2.21)	<0.05

BIA = bioelectrical impedance analysis, SEM = standard error of mean.

* Values are given as arithmetic means (SEM).

† Significant differences between porphyria patients and controls by unpaired Student *t* test.

(best imaginable health state) and a temporal equivalence (TE) index, indicating whether the subject's general state of health is perceived as being better, equal to or worse than over the past 12 months.⁷

The Barthel index, which is used to assess autonomy in the basic ADL, consists of the following 10 items: feeding, transfer, grooming, toilet use, bathing, mobility, stair climbing, dressing, bowel function, and bladder function. The level of assistance (ranging from complete assistance to independence) that was required for each item was scored on a 2 to 4-point scale in which a maximum level of assistance needed was scored as 0 and a minimum level of assistance needed was scored as 100.²⁰

The Katz index is used to assess functional status as a measurement of the patient's ability to perform ADL independently. The index ranks adequacy of performance in the 6 functions of bathing, dressing, toileting, transferring, continence, and feeding. Every activity is categorized to 3 levels of independence. In this categorization, people are included in 1 of the 7 levels of the index: from A (independent in all functions, with 6 the maximum value) to G (dependent on help for all 6 functions, with 0 the minimum value).^{21,22}

Statistical Analysis

Analyses were performed with the Statgraphics Centurion (version XVI) statistical program. Continuous variables were described as the mean value and standard error of mean (SEM). Significant differences in means were tested by unpaired Student *t* test. A 2-way analysis of variance (ANOVA) test (group × condition) was used to compare several anthropometric measurement values between ages (<50 years vs older), the

degree of adiposity (nonobese vs overweight and obese) with the study group (AIP vs control). Relative frequencies were given for noncontinuous variables. Significant differences in prevalence were calculated by means of χ^2 . The level of significance was established as $P < 0.05$.

RESULTS

Anthropometry

The anthropometric measurements for the AIP patients and their controls are shown in Table 1. Statistically significant higher mean values for knee-heel height, biiliac diameter, and CC were observed in AIP patients compared with control subjects. Leg length (tibia and fibula, main segment of height) was significantly greater in AIP patients than in the control group. AIP patients also showed significantly higher mean values of triceps skinfold and BIA than the control group. No significant differences in the other anthropometric measurements (ie, weight, height; biacromial, biepicondylar and bicondylar width diameters; arm, flexed midarm, waist and hip circumferences; subscapular, supraspinale, and calf skinfold thickness) were obtained when AIP and control groups were compared.

The interaction effect (2-way ANOVA) of 3 anthropometric parameters (knee-heel height, CC, and triceps skinfold thickness) for age (<50 years vs older) × study groups (ie, AIP vs control) was analyzed (Table 2). The mean knee-heel height was greater among AIP patients and those who were <50 years, although there was no statistically significant interaction between the 2 factors (age and AIP disease). So, shorter tibia

TABLE 2. Interaction Effect of 3 Anthropometric Parameters (Knee-Heel Height, Calf Circumference, and Triceps Skinfold Thickness) for Age (<50 y vs Older) × Study Groups (ie, Acute Intermittent Porphyria vs Control)*,†

Factors		Knee-heel height, cm	Calf circumference, cm	Triceps skinfold thickness, mm
Age, y	≤50	51.7 (0.8) [‡]	38.2 (1.1)	24.5 (2.1) [‡]
	>50	49.0 (0.8) [‡]	38.1 (1.1)	18.3 (2.1) [‡]
Disease	Porphyric	52.0 (0.8) [§]	40.4 (1.1) [§]	25.1 (2.1) [‡]
	Control	48.7 (0.8) [§]	35.9 (1.1) [§]	17.6 (2.1) [‡]

SEM = standard error of mean.

* Values are given as arithmetic means (SEM).

† Significant differences between groups by 2-factor analysis of variance. Component interaction is not significant.

‡ $P < 0.05$.§ $P < 0.01$.

length in older people was independent of the presence or absence of the diagnoses of AIP, which would reflect the different generations that the subjects belong to, rather than a decrease in the length of the long bones caused by aging.

Table 3 shows the anthropometric indicators for AIP and control groups. Differences in BMI bordered statistical significance, and were greater in the AIP group than in the control group. However, the BMI indicator could be affected by variations in height and leg length. Long leg bones (femur or tibia) are more closely related to stature than other bone segments and knee height appears to be independent of age and not to decrease over time.²³ So, the corrected BMI showed similar values for both the groups (AIP and control) and was close to the lower limit of being overweight (25.0 kg/m^2), according to the World Health Organization (WHO).²⁴ Knee-heel height was associated with overweight and was conditioned by the presence of AIP (2-way ANOVA) (Table 4), being $51.9 \pm 1.2 \text{ cm}$ for AIP patients and $48.7 \pm 0.9 \text{ cm}$ for the controls ($P < 0.05$).

There were no statistically significant difference in the Tanner Score, waist-to-hip ratio, body fat (%) calculated by triceps and/or subscapular skinfold thickness, arm muscle area (cm^2), and TMM (%) between AIP and control groups. The AIP group showed a significantly lower ponderal index (HWR) than the control group. With respect to the somatotype, the ectomorphy component, which reflects linearity in build,²⁵ was significantly lower in the AIP group, whereas the endomorphy component, which primarily reflects relative fatness or leanness,²⁵ was significantly higher in the AIP group than in the control group. The mesomorphy component, which reflects musculoskeletal development, did not differ across groups.

Health-Related Quality of Life

Table 5 shows health-related quality-of-life values obtained for each group (AIP and control) according to the EQ-5D health dimensions and indicators. The percentage of subjects who reported having “some problems” for mobility,

TABLE 3. Anthropometric Indicators for Acute Intermittent Porphyria Patients and Their Controls*,†

	Porphyria (n = 16)	Control (n = 16)	P values
BMI, kg/m^2	28.19 (0.83)	25.60 (1.07)	0.07
Corrected height, cm	168.21 (2.00)	162.48 (2.10)	0.06
BMI (corrected), kg/m^2	25.77 (0.90)	26.31 (1.01)	0.69
Tanner score	75.73 (2.59)	78.44 (1.65)	0.38
Waist-to-hip ratio	0.86 (0.02)	0.84 (0.02)	0.61
Body fat, % (triceps + subscapular)	32.38 (1.62)	29.05 (1.68)	0.16
Body fat, % (triceps)	31.06 (1.93)	26.06 (1.87)	0.07
Body fat, % (subscapular)	32.04 (1.47)	31.26 (1.54)	0.72
Arm muscle area, cm^2	34.24 (2.09)	36.37 (3.59)	0.61
Total muscle mass, %	27.33 (1.17)	30.39 (1.77)	0.16
HWR, $\text{cm/kg}^{0.33}$	38.53 (0.45)	40.32 (0.63)	<0.05
Endomorphy	7.12 (0.27)	5.79 (0.43)	<0.05
Mesomorphy	4.54 (0.43)	3.62 (0.46)	0.17
Ectomorphy	0.54 (0.15)	1.37 (0.31)	<0.05

BMI = body mass index, HWR = ponderal index (height/cube root of weight), SEM = standard error of mean.

* Values are given as arithmetic means (SEM).

† Significant differences between porphyria patients and controls by unpaired Student *t* test.

TABLE 4. Association of Anthropometric Parameters, Knee-Heel Height, Calf Circumference, and Triceps Skinfold Thickness, With the Degree of Adiposity (BMI 25 kg/m²) in the Study Population (Porphyric Patients and Control Group) and Disease in the Study Population (With Less or Over Adiposity of BMI 25 kg/m²)*,†

Factors		Knee-heel height, cm	Calf circumference, cm	Triceps skinfold thickness, mm
BMI, kg/m ²	≤25	50.2 (1.3)	35.7 (1.5)	21.6 (3.1)
	>25	50.4 (0.8)	39.0 (1.0)	21.2 (2.0)
Disease	Porphyric	51.9 (1.2) [‡]	39.0 (1.4)	25.0 (2.9)
	Control	48.7 (0.9) [‡]	35.8 (1.1)	17.7 (2.3)

BMI = body mass index, SEM = standard error of mean.

* Values are given as arithmetic means (SEM).

† Significant differences between groups by 2-way analysis of variance. Component interaction is not significant.

‡ $P < 0.05$.

self-care, usual activities, and “moderate” pain or discomfort was higher among the AIP group, whereas the percentage of subjects who reported to be in the “moderate” anxiety or depression level was higher in the control group than in the AIP group. Table 5 also shows the indicators of quality of life of the EQ-5D (VAS; Health State score, Index; and TE). Significant differences were only observed for VAS, with lower values in the AIP group than in the control group.

The level of dependency for each of the ADL of the study population, as measured by the Barthel index, is shown in

Table 6. No statistically significant differences were observed between the AIP and control groups. The overall results of the Barthel index showed that 81.25% of the porphyric group was independent, 6.25% showed a low level of dependency and 12.5% moderate dependency. In contrast, the control group showed total independence.

Table 6 also shows the degree of dependence for basic activities measured by the Katz index in the AIP and control groups. No statistically significant difference was obtained in the mean score between the 2 groups. As for the 6 activities that

TABLE 5. EuroQol-5D Health Dimensions Distribution Percentage Population and EuroQol-5D Indicators Scores in Acute Intermittent Porphyria Patients and Their Controls

Health dimensions (EuroQol-5D)		Porphyria (n = 16)	Control (n = 16)
1-Mobility, % [‡]	No problem	75.00	93.75
	Some problems	25.00	6.25
	Confined to bed	0.00	0.00
2-Self-care, % [‡]	No problem	87.50	100.00
	Some problems	12.50	0.00
	Unable to	0.00	0.00
3-Usual activities, % [‡]	No problem	75.00	87.50
	Some problems	25.00	12.50
	Unable to	0.00	0.00
4-Pain or discomfort, % [‡]	None	31.25	62.50
	Moderate	62.50	31.25
	Extreme	6.25	6.25
5-Anxiety or depression, % [‡]	None	68.75	37.50
	Moderate	31.25	56.25
	Extreme	0.00	6.25
Indicators EuroQol-5D*		P values [†]	
VAS (range 0–100), mean (SEM) [§]	61.56 (4.13)	76.56 (3.38)	<0.01
Index (range 0–1), mean (SEM) [§]	0.77 (0.05)	0.79 (0.04)	0.08
TE (range 0–1), mean (SEM) [§]	0.81 (0.06)	0.84 (0.05)	0.72

Index = health state score index, SEM = standard error of mean, TE = temporal equivalence, VAS = visual analog scale.

* Values are given as arithmetic means (SEM).

† Significant differences between porphyria patients and controls.

‡ By χ^2 .

§ By unpaired Student *t* test.

TABLE 6. Barthel and Katz Indices: Percentage of Population According to Independence in Activities of Daily Living in Acute Intermittent Porphyria Patients and Their Controls

Variable (range of scores)	Porphyria (n = 16)	Control (n = 16)	P values [†]
Barthel index (0–100) [‡]	98.1 (1.1)*	100.0 (0.0)*	0.1
Independent in all Barthel items, % [§]	93.75	100	
Feeding (10/5/0), % [§]	100/0/0	100/0/0	0.34
Bathing (5/0), % [§]	100/0	100/0	
Dressing (10/5/0), % [§]	93.75/6.25/0	100/0/0	
Stairs (10/5/0), % [§]	100/0/0	100/0/0	
Bladder (10/5/0), % [§]	100/0/0	100/0/0	
Bowels (10/5/0), % [§]	93.75/6.25/0	100/0/0	
Grooming (5/0), % [§]	93.75/6.25	100/0	
Toilet use (10/5/0), % [§]	100/0/0	100/0/0	
Transfer (15/10/5/0), % [§]	87.5/12.5/0/0	100/0/0/0	
Mobility (15/10/5/0), % [§]	93.75/6.25/0/0	100/0/0/0	
Katz index (0–6) [‡]	5.94 (0.06)*	6.00 (0.00)*	
Independent in all Katz items, % [‡]	93.75	100	
Independent in:			
Feeding, % [§]	100	100	
Bathing, % [§]	100	100	
Dressing, % [§]	100	100	
Continence, % [§]	93.75	100	
Transfer, % [§]	100	100	
Toileting, % [§]	100	100	

SEM = standard error of mean.

* Values are given as arithmetic means (SEM).

† Significant differences between porphyria patients and controls.

‡ By unpaired Student *t* test.§ No significant differences between the 2 populations were found by χ^2 .

assess the level of dependence, 93.75% of AIP patients were independent for all basic activities (level A). The remaining, 6.25% were considered dependent for 1 activity (continence) (level B). The control group showed independence in all items.

DISCUSSION

The main findings of the present study were that AIP patients showed statistically significant differences in terms of anthropometry (ie, knee-heel height, biiliac diameter, CC, triceps skinfold thickness, BIA, ponderal index, endomorphy, and ectomorphy) and in the quality of life by the EQ-5D questionnaire with respect to a control group.

Anthropometric Characteristics and Nutritional Status

The literature shows that nutritional status is directly related with variations in anthropometric measurements in humans, which confirms the importance of determining anthropometric measurements in the field of prevention, or for detecting or assessing individuals or populations at risk of malnutrition.^{26,27}

Acute porphyrias attacks can be triggered by fasting or carbohydrate restriction and are usually treated by the administration of glucose.^{2,28} The therapeutic intake of carbohydrates leads patients with AIP gaining weight. Furthermore, losing weight can be very difficult for these patients due to the risk of attacks induced by fasting.²⁸ In the present study, the results for BIA were higher in the porphyric patients than in the control.

BMI is an index of weight relative to height and mainly reflects energy balance. Midarm and CCs reflect subcutaneous fat and body muscle mass and are influenced by both energy balance and local muscle activity such as arm movement and walking activity. In cases of undernutrition, CC is a better indicator of body muscle mass because the legs contain over half of the muscle mass of the body. MAC reflects subcutaneous fat well but body muscle mass poorly because movement of the arms in daily activities occurs until very late stages of wasting, which helps maintain muscle mass locally.²⁹ Overall, BMI is a good indicator of weight change; CC is a good indicator of functional status; and MAC is a good indicator of terminal functional decline.⁵ In the present study, the results for CC pointed to higher mean value in the porphyric patients.

The most widely used indicator as an index of obesity is the BMI, but its main limitation is the inability to distinguish between fat mass and fat-free mass. It tends to indicate all the fat but not the distribution, whereas waist circumference values abdominal adiposity and skinfold thickness indicate the degree of adiposity and energy reserves distributed in different body regions. This is important because not only the total body fat but also its distribution plays an important role in the predisposition to certain diseases; for example, abdominal fat appears to be particularly relevant for cardiovascular and metabolic disease.^{13,30} In the present study, the skinfold (triceps) results pointed to greater subcutaneous fat deposits in the porphyric patients.

Somatotype analysis shows that in porphyric patients' endomorphy, a parameter that refers to body fat, was greater than ectomorphy, which is directly related to thinness. Several

studies have suggested a positive correlation between somatotype components and certain diseases.^{31,32} Similarly, our results show that anthropometric parameters such as ponderal index and somatotype components (endomorph, ectomorph) were conditioned by the presence of the disease.

Quality of Life

The HRQoL was described by means of the EQ-5D questionnaire. Other studies³³ showed a porphyric population distribution similar to our findings in this study, wherein the percentage of porphyric patients who reported having some problems (second level) was around 20% to 25 % with mobility and daily activities, but >35% for pain/discomfort and anxiety/depression. These results are consistent with the perception that porphyrics have of their disease and the symptoms associated with it, as indicated in the description of AIP given by Balwani and Desnick,² who mentioned that one of the main manifestations of the disease is abdominal pain due to visceral neuropathy. This is confirmed by the high percentage of the studied porphyric population (68.75%) who responded to the second and third level in the pain/discomfort dimension.

The quality of life reported by patients with chronic diseases is generally lower than in subjects without chronic diseases, and so higher values in the EQ-5D questionnaire are indicative of better quality of life. Thus, depression, cancer, and other diseases were seen to be predictors of risk in the VAS scale, with values <70, whereas for the general population (absence of chronic diseases), the observed score was higher.^{8,34} This is corroborated by the results of our study in which the porphyric population presented a mean value of 61.60 for the VAS.

Perneger et al³⁴ observed that health scores were lower among women, the elderly, those with basic education, users of health services, and those with lower self-reported health status, the population general showing a value of 0.83. In our study, the porphyric population showed values slightly lower (0.77) as the average age was 49.75 years.

Other questionnaires have been validated to study HRQoL, mostly multiitem scales reflecting ADL, and some provide subscales giving information on particular aspects, such as mobility and personal care.³⁵ Chronic diseases are often associated with a gradual dependence on others for ADL and with a growing need for care at home.^{36,37} The combination of measures such as the Barthel index and Katz index provide detailed information not only on the more or less independently performed ADL but also on how frequently the various activities were performed.³⁵

In the present study, scores for both indices provide conclusive evidence on the reduced dependence of porphyric patients. The WHO International Classification of Functioning, Disability, and Health describe disability in ADL as a multifactorial concept. ADL dependency is influenced by health conditions, body function and structures, and environmental and personal factors. Previous studies identified chronic diseases, physical activity, BMI, intraabdominal fat, atherosclerosis, sex, education, smoking, quality of life, and depressive symptoms as significant components of current ADL disability.³⁸ It follows that our study population did not have many of the factors that determine the level of ADL.

The relationship between quality of life, nutrition, and functionality is often complex. Torma et al³⁹ demonstrated that better nutritional status is significantly associated with better functional ability, including independent feeding and cognitive status. The authors found that those with a BMI >27 (similar to

our porphyric population) assessed their HRQoL as being higher than subjects with BMI <22. However, Bahat et al⁴⁰ observed that the correlation of BMI with ADL scores were more pronounced in females; Persson et al⁶ showed an increased Katz index in patients undergoing nutritional intervention with vitamin supplementation. However, there is some evidence of a nonlinear association between anthropometric parameters such as BMI and HRQL in patients with diabetes and coronary artery disease,⁴¹ although Hunger et al⁴² showed that BMI was significantly associated with EQ-5D questionnaire scores in persons with type 2 diabetes.

Similarly, in patients with osteoarthritis and other chronic diseases, Van Schoor et al⁴³ observed that of the 3 instruments used to assess HRQoL, the EQ-5D was the least sensitive for distinguishing changes in health perceived by the patients themselves. However, the EQ-5D is still considered a useful tool to measure HRQoL, as it integrates items of motor and functional disorders with emotional dysfunction.⁴⁴

Taking into account that many porphyria patients failed to be diagnosed within a short period of time, the EQ-5D test could contribute to identifying the presence or help follow the evolution of the disease as it has been demonstrated that quality-of-life factors are significantly abnormal in porphyria patients.³²

CONCLUSION

According to our results and those obtained assessing nutritional status of the porphyric population³ and taking into account the characteristics concerning their carbohydrate needs and, more specifically, the role of glucose intake in preventing acute attacks of porphyria, anthropometric parameters and their relationship with glucose levels should be taken into account when considering a possible therapy that can control the symptoms of the disease and thus improve patients' autonomy.

It is deduced from the results obtained that the parameter VAS in EQ-5D can discriminate the presence of porphyria. AIP patients showed a high degree of independence in the ADL when assessed by the Barthel and Katz tests.

ACKNOWLEDGMENT

The authors would like to thank Dr Carvalho de Vasconcelos and his group for their critical review of the manuscript.

REFERENCES

- Guillén-Navarro E, Carbonell P, Glover G, et al. Novel HMBS founder mutation and significant intronic polymorphism in Spanish patients with acute intermittent Porphyria. *Ann Hum Genet.* 2004;68:509–514.
- Balwani M, Desnick R. The porphyrias: advances in diagnosis and treatment. *Blood.* 2012;120:4496–4504.
- García-Diz L, Murcia MA, Gris JL, et al. Assessing nutritional status of acute intermittent porphyria patients. *Eur J Clin Invest.* 2012;42:943–952.
- Wyka J, Biernat J, Kiedik D. Nutritional determination of the health status in Polish elderly people from an urban environment. *J Nutr Health Aging.* 2010;14:67–71.
- Tsai A, Lai M-C, Chang T-L. Mid-arm calf circumferences (MAC and CC) are better than body mass index (BMI) in predicting health status and mortality risk in institutionalized elderly Taiwanese. *Arch Gerontol Geriatr.* 2012;54:443–447.
- Persson M, Hytten-Landahl A, Brismar K, et al. Nutritional supplementation and dietary advice in geriatric patients at risk of malnutrition. *Clin Nutr.* 2007;26:216–224.

7. Kvamme J, Olsen J, Florhlmén J, et al. Risk of malnutrition and health-related quality of life in community-living elderly men and women: the Tromsø study. *Qual Life Res*. 2011;20:575–582.
8. Wang H-M, Beyer M, Gensinchen J, et al. Health-related quality of life among general practice patients with differing chronic diseases in Germany: cross sectional survey. *BMC Public Health*. 2008;8:1–12.
9. Pinto E, Maso I, Ribeiro R, et al. Validation of the EuroQol quality of life questionnaire on stroke victims. *Arq Neuropsiquiatr*. 2011;69:320–323.
10. Cabañero-Martínez MJ, Cabrero-García J, Richart-Martínez M, et al. The Spanish versions of the Barthel index (BI) and the Katz index (KI) of activities of daily living (ADL): a structured review. *Arch Gerontol Geriatr*. 2009;49:77–84.
11. Pimentel G, Portero-McLellan KC, Maestá N, et al. Accuracy of sagittal abdominal diameter as predictor of abdominal fat among Brazilian adults: a comparison with waist circumference. *Nutr Hosp*. 2010;25:656–661.
12. World Health Organization (WHO). Physical status: the use and interpretation of anthropometry. Report of a WHO expert committee 854. Geneva: World Health Organization; 1995.
13. Katz P, Gregorich S, Yazdany J, et al. Obesity and its measurement in a community based sample of women with systemic lupus erythematosus. *Arthritis Care Res*. 2011;63:261–268.
14. Kraemer-Aguiar LG, Maranhao PA, Sicuro FL, et al. Microvascular dysfunction: a direct among BMI, waist circumference and glucose homeostasis in young overweight/obese normoglycemic women? *Int J Obesity*. 2010;34:111–117.
15. Chumlea WC, Guo SS, Wholihan K, et al. Stature prediction equations for elderly non-Hispanic white, non-Hispanic black and Mexican-American persons developed from NHANES III data. *J Am Diet Assoc*. 1998;98:137–142.
16. Haugaard SB, Vaag A, Hoy C, et al. Sex and muscle structural lipids in obese subjects: an impact on insulin action? *Eur J Clin Invest*. 2008;38:494–501.
17. Corvalán C, Uauy R, Kain J, et al. Obesity indicators and cardiometabolic status in 4-y-old children. *Am J Clin Nutr*. 2010;91:166–174.
18. Rutters F, Nieuwenhuizen A, Lemmens S, et al. Hypothalamic pituitary adrenal (HPA) axis functioning in relation to body fat distribution. *Clin Endocrinol*. 2010;72:738–743.
19. Ronco AL, Mendoza B, Varas X, et al. Somatotype and risk of breast cancer: a case-control study in Uruguay. *Rev Bras Epidemiol*. 2008;11:215–227.
20. Kitamura K, Nakamura K, Nishiwaki T, et al. Low body mass index and low serum albumin are predictive factors for short-term mortality in elderly Japanese requiring home care. *Tohoku J Exp Med*. 2010;221:29–34.
21. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc*. 1983;31:721–727.
22. Cieri E, Lenti M, De Rando P, et al. Functional ability in patients with critical limb ischaemia is unaffected by successful revascularisation. *Eur J Vasc Endovasc Surg*. 2011;41:256–263.
23. Cereda E, Bertoli S, Battezzati A. Height prediction formula for middle-aged (30–35 y) Caucasians. *Nutr*. 2010;26:1075–1081.
24. World Health Organization (WHO). Report of a WHO Consultation on Obesity. Obesity: preventing and managing the global epidemic. Geneva: World Health Organization; 1998.
25. Behaein B, Yadolazadeh A, Same H, et al. Relation of anthropometric characteristics in women with different types of MS and comparison with health ones. *Ann Biol Res*. 2011;2:14–21.
26. Beberashvili I, Azar A, Sinuani I, et al. Objective score of nutrition on dialysis as an alternative for the malnutrition inflammation score in assessment of nutritional risk of haemodialysis patients. *Nephrol Dial Transplant*. 2010;25:2662–2671.
27. Pimentel G, Arimura S, de Moura B, et al. Short term nutritional counseling reduces body mass index, waist circumference, triceps skinfold and triglycerides in women with metabolic syndrome. *Diabetol Metab Syndr*. 2010;2:1–7.
28. Oliveri L, Davio C, Batlle A, et al. ALAS1 gene expression is down-regulated by Akt-mediated phosphorylation and nuclear exclusion of FOXO1 by vanadate in diabetic mice. *Biochem J*. 2012;442:303–310.
29. Chumlea WC. Is the MNA valid in different populations and across practice settings? *J Nutr Health Aging*. 2006;10:524–533.
30. Amato M, Guarnotta V, Giordano C. Body composition assessment for the definition of cardiometabolic risk. *J Endocrinol Invest*. 2013;36:537–543.
31. Baltadjiev A. Somatotype characteristics of male patients with type 2 diabetes mellitus. *Folia Medica*. 2012;54:40–45.
32. Mager D, Yap J, Rodriguez-Dimitrescu C, et al. Anthropometric measures of visceral and subcutaneous fat are important in the determination of metabolic dysregulation in boys and girls at risk for non-alcoholic fatty liver disease. *Nutr Clin Practice*. 2013;28:101–111.
33. Millward LM, Kelly P, Deacon A, et al. Self-rate psychosocial consequences and quality of life in the acute porphyrias. *J Inherit Metab Dis*. 2001;24:733–747.
34. Perneger T, Combescuré C, Courvoisier D. general population reference values for the French version of the EuroQol EQ-5D health utility instrument. *Value Health*. 2010;13:631–635.
35. Buurman B, Munster B, Korevaar J, et al. Variability in measuring (instrumental) activities of daily living functional decline in hospitalized older medical patients: a systematic review. *J Clin Epidemiol*. 2011;64:619–627.
36. Hoogerduijn JG, Schuurmans MJ, Korevaar JC, et al. Identification of older hospitalised patients at risk for functional decline, a study to compare the predictive values of three screening instruments. *J Clin Nurs*. 2010;19:1219–1225.
37. Ploughman M, Austin M, Stefanelli M, et al. Applying cognitive debriefing to pre-test patient reported outcomes in older people with multiple sclerosis. *Qual Life Res*. 2010;19:483–487.
38. Ouden M, Schuurmans M, Mueller-Schotte S, et al. Domains contributing to disability in activities of daily living. *J Am Directors Ass*. 2013;14:18–24.
39. Törma J, Winblad U, Cederholm T, et al. Does undernutrition still prevail among nursing home residents? *Clin Nutr*. 2013;32:562–568.
40. Bahat G, Tufan F, Saka B, et al. Which body mass index (BMI) is better in the elderly for functional status? *Arch Gerontol Geriatr*. 2012;54:78–81.
41. Hlatky MA, Chung SC, Escobedo J, et al. The effect of obesity on quality of life in patients with diabetes and coronary artery disease. *Am Heart J*. 2010;159:292–300.
42. Hunger M, Schunk M, Meisinger C, et al. Estimation of the relationship between body mass index and EQ-5D health utilities in individuals with type 2 diabetes: evidence from the population-based KORA studies. *J Diabetes Complicat*. 2012;26:413–418.
43. Van Schoor NM, Smit JH, Twisk JWR. Impact of vertebral deformities, osteoarthritis, and other chronic diseases on quality of life: a population-based study. *Osteoporos Int*. 2005;16:749–756.
44. De Wit L, Molas M, Dejaeger E, et al. The use of a biplot studying outcomes after stroke. *Neurorehabil Neural Repair*. 2009;23:825–830.